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3. In the drawings, any words are not translated.

CLAIMS

[Claim(s)]

[Claim 1] It is a liquid constituent for delivery of the activity matter biologically. : Liquid constituent containing the liquid carrier ingredient of the hyperviscosity of nonaqueous solubility which has the viscosity of 5,000cP(s) at least at 37 degrees C, and is not crystallized in the flesh under a perimeter or physiological conditions including the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1.

[Claim 2] The constituent according to claim 1 whose at least one of the aforementioned carboxylic acids of at least 1 is a hydroxy acid.

[Claim 3] The constituent according to claim 1 with which aforementioned non-giant-molecule ester or mixed ester is obtained by the ring opening reaction of lactone or annular carbonate.

[Claim 4] The constituent according to claim 2 with which aforementioned non-macromolecule ester or mixed ester contains the hydroxy-acid parts of 2 - abbreviation 20.

[Claim 5] The constituent according to claim 3 with which aforementioned non-macromolecule ester or mixed ester contains the hydroxy-acid parts of 2 - abbreviation 20.

[Claim 6] The constituent according to claim 1 with which the aforementioned non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 contains the polyoxy alcoholic part which has the hydroxy parts of 2 - abbreviation 20.

[Claim 7] The constituent according to claim 1 with which aforementioned non-giant-molecule ester or mixed ester contains the alcoholic part which has the end hydroxy part of at least 1 esterified with the carboxylic acid obtained according to the alcoholysis of a carboxylic anhydride.

[Claim 8] The constituent according to claim 7 whose aforementioned carboxylic anhydride is a cyclic anhydride.

[Claim 9] The constituent according to claim 1 with which aforementioned non-macromolecule ester or mixed ester contains the alcoholic part which has the end hydroxy part of at least 1 esterified with amino acid.

[Claim 10] The constituent containing the alcoholic part obtained by removing at least one hydrogen atom from the alcohol chosen from the group to which aforementioned non-macromolecule ester or mixed ester becomes monofunctional nature C1 - C20 alcohol, bifunctional C 1 - C20 alcohol, trifunctional alcohol, a hydroxy content carboxylic acid, hydroxy content amino acid, phosphate content alcohol, tetrafunctional alcohol, sugar-alcohol, monosaccharide and disaccharide, and a saccharic acid list from polyether polyol according to claim 6.

[Claim 11] The constituent according to claim 10 whose monofunctional nature C1 - C20 alcohol is a dodecanol.

[Claim 12] The constituent according to claim 10 whose bifunctional C 1 - C20 alcohol is hexandiol.

[Claim 13] The constituent according to claim 10 whose trifunctional alcohol is glycerol.

[Claim 14] The constituent according to claim 10 whose hydroxy content carboxylic acids are a glycolic acid, lactic acids, or these combination.

[Claim 15] The constituent according to claim 10 whose hydroxy content amino acid is a serine.

[Claim 16] The constituent according to claim 10 whose hydroxy content acids are hydroxybutyric acid, a hydroxy valeric acid, hydroxy caproic acids, or such mixture of at least 1.

[Claim 17] The constituent according to claim 10 whose phosphate content alcohol is ATP.

[Claim 18] The constituent according to claim 10 whose tetrafunctional alcohol is a pentaerythritol.

[Claim 19] The constituent according to claim 10 whose sugar-alcohol is a mannitol or a sorbitol.

[Claim 20] The constituent according to claim 10 whose monosaccharide is a glucose or a fructose.

[Claim 21] The constituent according to claim 10 whose disaccharide is shoe cloth.

[Claim 22] The constituent according to claim 10 whose saccharic acid is glucuronic acid.

[Claim 23] The constituent according to claim 10 polyether polyol is the poly glycerol ether containing the glycerol unit of 1 - abbreviation 10, or is [constituent] a polyethylene glycol containing the ethylene glycol unit of 1 - abbreviation 20.

[Claim 24] The constituent according to claim 3 which chooses lactone from the group which consists of glycolide, a lactide, epsilon-caprolactone, a butyrolactone, and a valerolactone, and chooses annular carbonate from the group which consists of trimethylene carbonate and propylene carbonate.

[Claim 25] The constituent according to claim 1 which contains the activity matter further biologically.

[Claim 26] The aforementioned constituent according to claim 25 which carried out the encapsulation of the activity matter to the microsphere biologically.

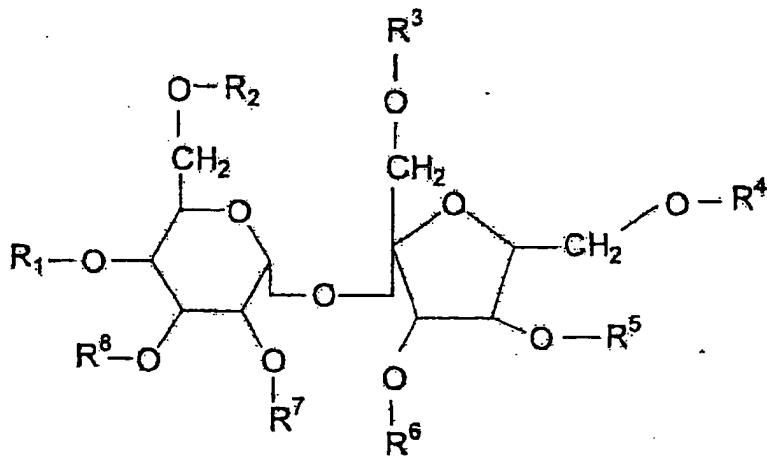
[Claim 27] The constituent according to claim 25 which chooses the activity matter from the group which consists of protein, a peptide, a nucleoprotein, mucoprotein, a lipoprotein, and synthetic polypeptide biologically.

[Claim 28] The constituent according to claim 27 which chooses protein from the group which consists of human growth hormone, fibroblast growth factor (FGF), erythropoietin (EPO), platelet derived growth factor (PDGF), granulocyte colony-stimulating factor (g-CSF), cow somatotropin (BST), tumor necrosis factor (TNF), and transforming growth factor beta (TGF-beta), interleukin, an insulin, and interferon.

[Claim 29] The constituent according to claim 25 which chooses the activity matter from the group which consists of a nucleic acid, a nucleotide, a nucleoside, an oligonucleotide, and a gene biologically.

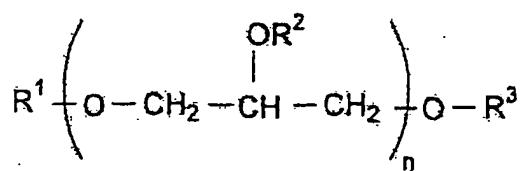
[Claim 30] The constituent according to claim 29 with which a nucleic acid contains DNA, RNA, or these fragments.

[Claim 31] Liquid constituent:I according to claim 1 which has the structure chosen from the group which a hyperviscous liquid carrier ingredient becomes from the following: [Formula 1]

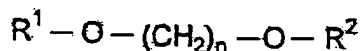


(R1, R2, R3, R4, R5, R6, R7, and R8 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);
 (At least three, R1, R2, R3, R4, R5, R6, R7, and R8, among a formula) it is except hydrogen --;, and

(R1, R2, R3, R4, R5, R6, R7, and R8 are chosen from the group which consists of acetyl and isobutyryl among a formula, and at least three, R1, R2, R3, R4, R5, R6, R7, and R8, are acetyl);
 II: [Formula 2]

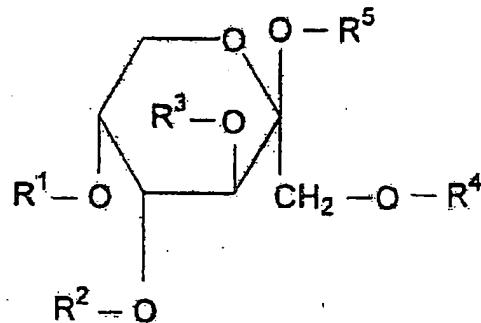


(Choosing independently R1, R2, and R3 from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula, n is 1-20); III : [Formula 3]

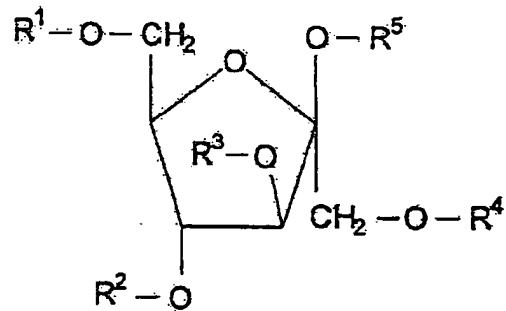


(n is the integer of 4-8 among a formula, and R1 and R2 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out);

IV: [Formula 4]

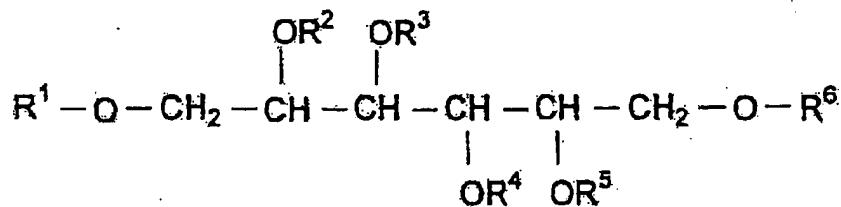


V: [Formula 5]

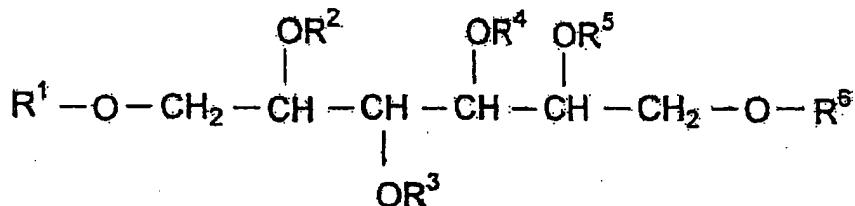


(R1, R2, R3, R4, and R5 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);

VI: [Formula 6]

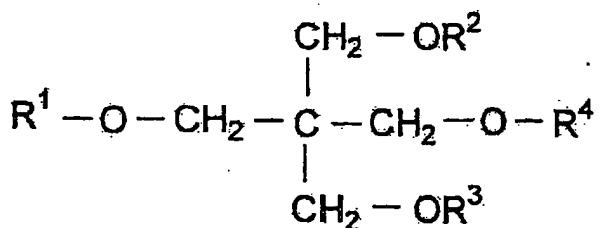


VII: [Formula 7]



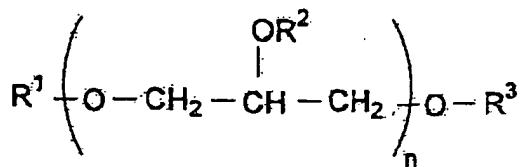
(R1, R2, R3, R4, R5, and R6 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);

VIII: [Formula 8]



(R1, R2, R3, and R4 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula).

[Claim 32] A constituent including the structure chosen from the group which a hyperviscous liquid carrier becomes from the following according to claim 31: [Formula 9]

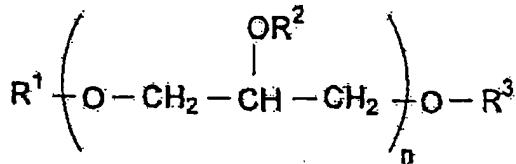


(n is 1 among a formula and R1, R2, and R3 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out); and [Formula 10]



(n is 6 among a formula and R1 and R2 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out).

[Claim 33] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 11]



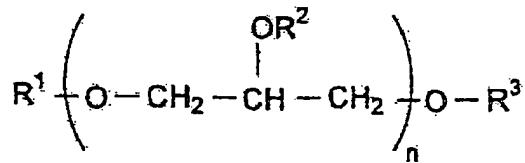
(n is 1 among a formula and at least one of R1, R2, and the R3 is independently chosen from the group which consists of alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out).

[Claim 34] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of lactoyl, the poly lactoyl, epsilon-caproyl, hydroxy acetyl, and polyhydroxy acetyl.

[Claim 35] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of poly lactoyl and epsilon-caproyl.

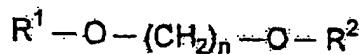
[Claim 36] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of poly lactoyl and polyhydroxy acetyl.

[Claim 37] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 12]



(n is 1 among a formula, at least one of R1, R2, and the R3 is independently chosen from the group which consists of alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out, and these have 2 - 4 carbon atom respectively).

[Claim 38] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 13]



(n is 6 among a formula and R1 and R2 are independently chosen from the group which consists of lactoyl, the poly lactoyl, epsilon-caproyl, hydroxy acetyl, and polyhydroxy acetyl).

[Claim 39] The constituent according to claim 38 which chooses R1 and R2 from the group which consists of poly lactoyl and epsilon-caproyl independently.

[Claim 40] The constituent according to claim 38 which chooses R1 and R2 from the group which consists of poly lactoyl and polyhydroxy acetyl independently.

[Claim 41] The constituent according to claim 1 which contains the solvent of a hyperviscous liquid carrier ingredient further.

[Claim 42] A solvent An acetone, benzyl alcohol, benzyl benzoate, N-(beta hydronium methyl) RAKUTAMIDO, A butylene glycol, a caprolactam, a caprolactone, corn oil, DESHIRU methyl sulfoxide, wood ether, dimethyl sulfoxide, 1-dodecylazacycloheptane-2-one, ethanol, ethyl acetate, Ethyllactate, ethyl oleate, glycerol, the Glico furol (tetra-glycol), The isopropyl myristate, methyl acetate, a methyl ethyl ketone, A N-methyl-2-pyrrolidone, a caprylic acid and/or a capric acid, glycerol, or ester with alkylene glycol, Oleic acid, peanut oil, a polyethylene glycol, propylene carbonate, The 2-pyrrolidone, sesame oil, [**]-2, and 2-dimethyl -1, a 3-dioxolane-4-methanol,

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CLAIMS

[Claim(s)]

[Claim 1] It is a liquid constituent for delivery of the activity matter biologically. : Liquid constituent containing the liquid carrier ingredient of the hyperviscosity of nonaqueous solubility which has the viscosity of 5,000cP(s) at least at 37 degrees C, and is not crystallized in the flesh under a perimeter or physiological conditions including the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1.

[Claim 2] The constituent according to claim 1 whose at least one of the aforementioned carboxylic acids of at least 1 is a hydroxy acid.

[Claim 3] The constituent according to claim 1 with which aforementioned non-giant-molecule ester or mixed ester is obtained by the ring opening reaction of lactone or annular carbonate.

[Claim 4] The constituent according to claim 2 with which aforementioned non-macromolecule ester or mixed ester contains the hydroxy-acid parts of 2 - abbreviation 20.

[Claim 5] The constituent according to claim 3 with which aforementioned non-macromolecule ester or mixed ester contains the hydroxy-acid parts of 2 - abbreviation 20.

[Claim 6] The constituent according to claim 1 with which the aforementioned non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 contains the polyoxy alcoholic part which has the hydroxy parts of 2 - abbreviation 20.

[Claim 7] The constituent according to claim 1 with which aforementioned non-giant-molecule ester or mixed ester contains the alcoholic part which has the end hydroxy part of at least 1 esterified with the carboxylic acid obtained according to the alcoholysis of a carboxylic anhydride.

[Claim 8] The constituent according to claim 7 whose aforementioned carboxylic anhydride is a cyclic anhydride.

[Claim 9] The constituent according to claim 1 with which aforementioned non-macromolecule ester or mixed ester contains the alcoholic part which has the end hydroxy part of at least 1 esterified with amino acid.

[Claim 10] The constituent containing the alcoholic part obtained by removing at least one hydrogen atom from the alcohol chosen from the group to which aforementioned non-macromolecule ester or mixed ester becomes monofunctional nature C1 - C20 alcohol, bifunctional C 1 - C20 alcohol, trifunctional alcohol, a hydroxy content carboxylic acid, hydroxy content amino acid, phosphate content alcohol, tetrafunctional alcohol, sugar-alcohol, monosaccharide and disaccharide, and a saccharic acid list from polyether polyol according to claim 6.

[Claim 11] The constituent according to claim 10 whose monofunctional nature C1 - C20 alcohol is a dodecanol.

[Claim 12] The constituent according to claim 10 whose bifunctional C 1 - C20 alcohol is hexandiol.

[Claim 13] The constituent according to claim 10 whose trifunctional alcohol is glycerol.

[Claim 14] The constituent according to claim 10 whose hydroxy content carboxylic acids are a glycolic acid, lactic acids, or these combination.

[Claim 15] The constituent according to claim 10 whose hydroxy content amino acid is a serine.

[Claim 16] The constituent according to claim 10 whose hydroxy content acids are hydroxybutyric acid, a hydroxy valeric acid, hydroxy caproic acids, or such mixture of at least 1.

[Claim 17] The constituent according to claim 10 whose phosphate content alcohol is ATP.

[Claim 18] The constituent according to claim 10 whose tetrafunctional alcohol is a pentaerythritol.

[Claim 19] The constituent according to claim 10 whose sugar-alcohol is a mannitol or a sorbitol.

[Claim 20] The constituent according to claim 10 whose monosaccharide is a glucose or a fructose.

[Claim 21] The constituent according to claim 10 whose disaccharide is shoe cloth.

[Claim 22] The constituent according to claim 10 whose saccharic acid is glucuronic acid.

[Claim 23] The constituent according to claim 10 polyether polyol is the poly glycerol ether containing the glycerol unit of 1 - abbreviation 10, or is [constituent] a polyethylene glycol containing the ethylene glycol unit of 1 - abbreviation 20.

[Claim 24] The constituent according to claim 3 which chooses lactone from the group which consists of glycolide, a lactide, epsilon-caprolactone, a butyrolactone, and a valerolactone, and chooses annular carbonate from the group which consists of trimethylene carbonate and propylene carbonate.

[Claim 25] The constituent according to claim 1 which contains the activity matter further biologically.

[Claim 26] The aforementioned constituent according to claim 25 which carried out the encapsulation of the activity matter to the microsphere biologically.

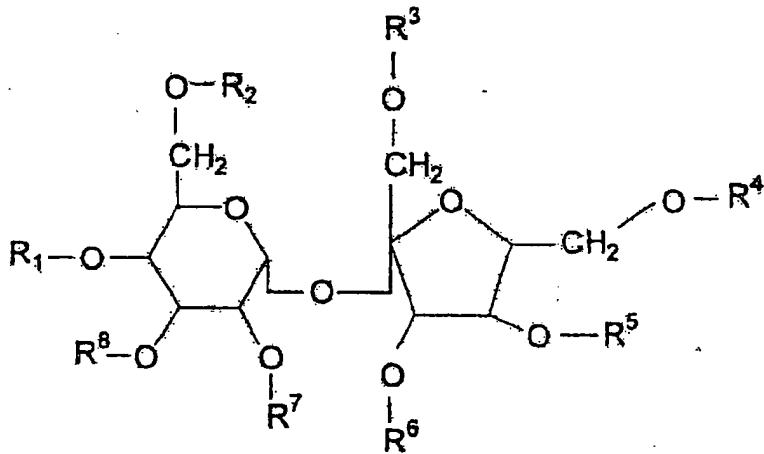
[Claim 27] The constituent according to claim 25 which chooses the activity matter from the group which consists of protein, a peptide, a nucleoprotein, mucoprotein, a lipoprotein, and synthetic polypeptide biologically.

[Claim 28] The constituent according to claim 27 which chooses protein from the group which consists of human growth hormone, fibroblast growth factor (FGF), erythropoietin (EPO), platelet derived growth factor (PDGF), granulocyte colony-stimulating factor (g-CSF), cow somatotropin (BST), tumor necrosis factor (TNF), and transforming growth factor beta (TGF-beta), interleukin, an insulin, and interferon.

[Claim 29] The constituent according to claim 25 which chooses the activity matter from the group which consists of a nucleic acid, a nucleotide, a nucleoside, an oligonucleotide, and a gene biologically.

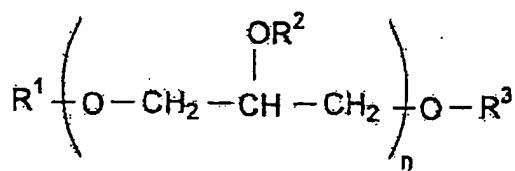
[Claim 30] The constituent according to claim 29 with which a nucleic acid contains DNA, RNA, or these fragments.

[Claim 31] Liquid constituent:I according to claim 1 which has the structure chosen from the group which a hyperviscous liquid carrier ingredient becomes from the following: [Formula 1]

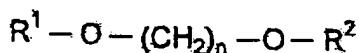


(R1, R2, R3, R4, R5, R6, R7, and R8 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);
 (At least three, R1, R2, R3, R4, R5, R6, R7, and R8, among a formula) it is except hydrogen --;, and

(R1, R2, R3, R4, R5, R6, R7, and R8 are chosen from the group which consists of acetyl and isobutyryl among a formula, and at least three, R1, R2, R3, R4, R5, R6, R7, and R8, are acetyl);
 II: [Formula 2]

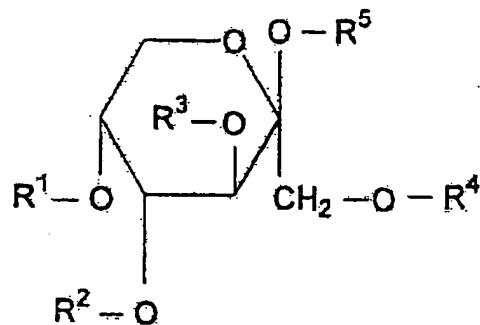


(Choosing independently R1, R2, and R3 from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula, n is 1-20); III : [Formula 3]

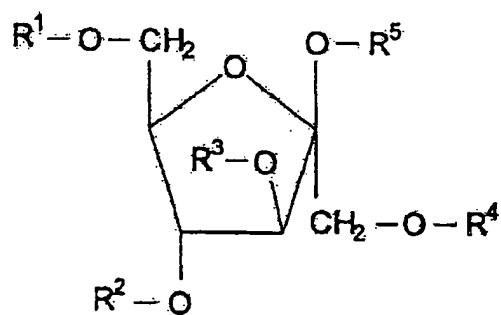


(n is the integer of 4-8 among a formula, and R1 and R2 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out);

IV: [Formula 4]

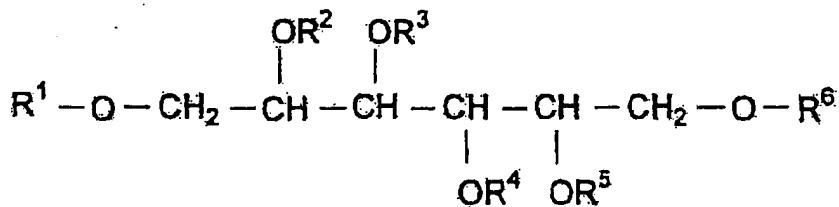


V: [Formula 5]

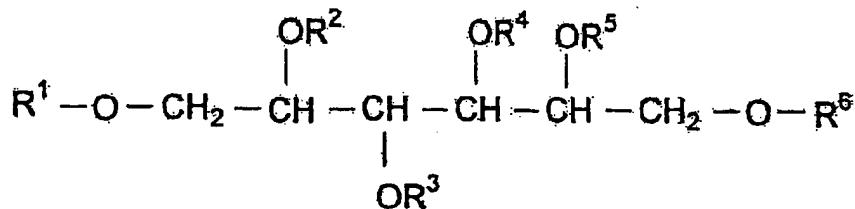


(R1, R2, R3, R4, and R5 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);

VI: [Formula 6]

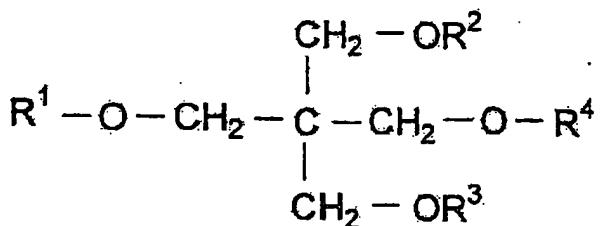


VII: [Formula 7]



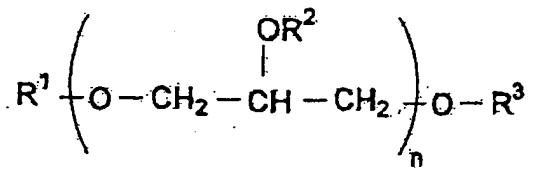
(R1, R2, R3, R4, R5, and R6 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);

VIII: [Formula 8]



(R1, R2, R3, and R4 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula).

[Claim 32] A constituent including the structure chosen from the group which a hyperviscous liquid carrier becomes from the following according to claim 31: [Formula 9]

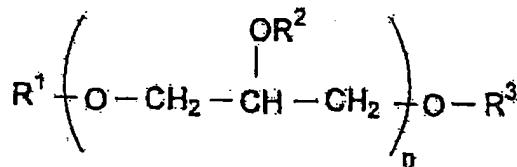


(n is 1 among a formula and R1, R2, and R3 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out); and [Formula 10]



(n is 6 among a formula and R1 and R2 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out).

[Claim 33] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 11]



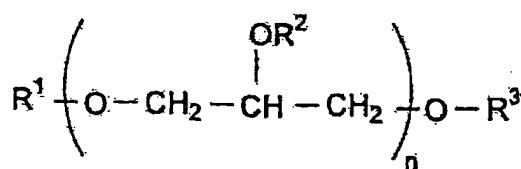
(n is 1 among a formula and at least one of R1, R2, and the R3 is independently chosen from the group which consists of alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out).

[Claim 34] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of lactoyl, the poly lactoyl, epsilon-caproyl, hydroxy acetyl, and polyhydroxy acetyl.

[Claim 35] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of poly lactoyl and epsilon-caproyl.

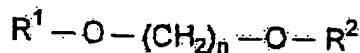
[Claim 36] The constituent according to claim 33 which chooses independently R1, R2, and R3 from the group which consists of poly lactoyl and polyhydroxy acetyl.

[Claim 37] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 12]



(n is 1 among a formula, at least one of R1, R2, and the R3 is independently chosen from the group which consists of alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out, and these have 2 - 4 carbon atom respectively).

[Claim 38] The constituent according to claim 32 with which a hyperviscous liquid carrier includes the following structure: [Formula 13]



(n is 6 among a formula and R1 and R2 are independently chosen from the group which consists of lactoyl, the poly lactoyl, epsilon-caproyl, hydroxy acetyl, and polyhydroxy acetyl).

[Claim 39] The constituent according to claim 38 which chooses R1 and R2 from the group which consists of poly lactoyl and epsilon-caproyl independently.

[Claim 40] The constituent according to claim 38 which chooses R1 and R2 from the group which consists of poly lactoyl and polyhydroxy acetyl independently.

[Claim 41] The constituent according to claim 1 which contains the solvent of a hyperviscous liquid carrier ingredient further.

[Claim 42] A solvent An acetone, benzyl alcohol, benzyl benzoate, N-(beta hydronium methyl) RAKUTAMIDO, A butylene glycol, a caprolactam, a caprolactone, corn oil, DESHIRU methyl sulfoxide, wood ether, dimethyl sulfoxide, 1-dodecylazacycloheptane-2-one, ethanol, ethyl acetate, Ethyllactate, ethyl oleate, glycerol, the Glico furol (tetra-glycol), The isopropyl myristate, methyl acetate, a methyl ethyl ketone, A N-methyl-2-pyrrolidone, a caprylic acid and/or a capric acid, glycerol, or ester with alkylene glycol, Oleic acid, peanut oil, a polyethylene glycol, propylene carbonate, The 2-pyrrolidone, sesame oil, [**]-2, and 2-dimethyl -1, a 3-dioxolane-4-methanol, The constituent according to claim 41 chosen from a tetrahydrofuran, diethylene glycol monoethyl ether, carbitol, a triacetin, triethyl SHITORETO, and the group that consists of these combination.

[Claim 43] The constituent according to claim 41 which chooses a solvent from the group which consists of trichlorofluoromethane, fluoro carbon 21, tetrafluoro ethane (R-134a), wood ether, a propane, butane, and these combination.

[Claim 44] The constituent according to claim 41 which chooses a solvent from benzyl benzoate, dimethyl sulfoxide, ethanol, ethyllactate, glycerol, the Glico furol (tetra-glycol), a N-methyl-2-pyrrolidone, capryl lactam / capric-acid triglyceride, a polyethylene glycol, propylene carbonate, 2-pyrrolidone, and the group that consists of these combination.

[Claim 45] The constituent according to claim 1 which carried out the encapsulation of the constituent to the microsphere.

[Claim 46] The constituent according to claim 1 with which the encapsulation of the constituent was carried out to the microsphere and which contains the activity matter further biologically.

[Claim 47] The constituent according to claim 1 whose constituent is a milky lotion gestalt.

[Claim 48] The constituent according to claim 1 which contains an additive further.

[Claim 49] The constituent according to claim 48 which chooses an additive from the group which consists of a biodegradability polymer, the polymer which is not biodegradability, natural oil, synthetic oil, a carbohydrate, a carbohydrate derivative, mineral, an inactive organic compound, and water.

[Claim 50] It is the approach of medicating with the activity matter biologically the vegetation or animal which needs it : To this vegetation or an animal Liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility which has the viscosity of 5,000cP(s) at least at 37 degrees C including a kind of non-macromolecule ester or mixed ester of a carboxylic acid, and is not crystallized under a perimeter or physiological conditions in the flesh;

The above-mentioned approach including prescribing the constituent containing activity matter and; for the patient biologically.

[Claim 51] The approach according to claim 50 a constituent contains further the solvent whose liquid carrier ingredient of the hyperviscosity of nonaqueous solubility is fusibility.

[Claim 52] The approach according to claim 51 of the aforementioned solvent being spread from the liquid carrier ingredient of the hyperviscosity of the aforementioned nonaqueous solubility, or moving,

and including further that the viscosity of a constituent increases by that cause.

[Claim 53] The aforementioned approach according to claim 50 of emitting the activity matter with time during the tissue of vegetation or an animal from the constituent biologically [the aforementioned constituent].

[Claim 54] The approach according to claim 50 the aforementioned administration includes administration by injection.

[Claim 55] The approach according to claim 50 the aforementioned administration includes rectum administration.

[Claim 56] The approach according to claim 50 the aforementioned administration includes the administration in a vagina.

[Claim 57] The approach according to claim 50 the aforementioned administration includes the administration in a nasal cavity.

[Claim 58] The approach according to claim 50 the aforementioned administration includes partial administration.

[Claim 59] The approach according to claim 50 the aforementioned administration includes lung administration.

[Claim 60] They are the transplantation object for internal medicine or surgery, the film, or a transplant constituent. : The above-mentioned constituent containing the liquid carrier ingredient of the hyperviscosity of nonaqueous solubility which has the viscosity of 5,000cP(s) at least at 37 degrees C, and is not crystallized under a perimeter or physiological conditions in the flesh including the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1.

[Claim 61] The internal medicine according to claim 60 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule has the viscosity of 10,000cP(s) at least at 37 degrees C, the film, or a transplant constituent.

[Claim 62] The internal medicine according to claim 61 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule has the viscosity of 15,000cP(s) at least at 37 degrees C, the film, or a transplant constituent.

[Claim 63] The internal medicine according to claim 62 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule has the viscosity of 20,000cP(s) at least at 37 degrees C, the film, or a transplant constituent.

[Claim 64] The internal medicine according to claim 63 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule has the viscosity of 25,000cP(s) at least at 37 degrees C, the film, or a transplant constituent.

[Claim 65] The internal medicine according to claim 64 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule has the viscosity of 30,000cP(s) at least at 37 degrees C, the film, or a transplant constituent.

[Claim 66] The internal medicine according to claim 60 or the transplantation object for surgery with which the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule contains an additive further, the film, or a transplant constituent.

[Claim 67] The internal medicine according to claim 66 or the transplantation object for surgery which chooses an additive from the group which consists of water, a biodegradability polymer or oligomer, the polymer that is not biodegradability or oligomer, natural oil, synthetic oil, a carbohydrate, a carbohydrate derivative, mineral, and an inactive organic compound, the film, or a transplant constituent.

[Claim 68] The internal medicine according to claim 60 or the transplantation object for surgery which contains the activity matter further biologically, film, or transplant constituent for the controlled

delivery.

[Claim 69] The internal medicine according to claim 60 or the transplantation object for surgery which is the block over surgical adhesion, the film, or a transplant constituent.

[Claim 70] The internal medicine according to claim 60 or the transplantation object for surgery which is the dead-air-space filler of a living thing in-house, the film, or a transplant constituent.

[Claim 71] The internal medicine according to claim 60 or the transplantation object for surgery which is the guide of anagenesis, the film, or a transplant constituent.

[Claim 72] The internal medicine according to claim 60 or the transplantation object for surgery which is hemostasis material, the film, or a transplant constituent.

[Claim 73] The internal medicine according to claim 60 or the transplantation object for surgery which is tissue adhesives, the film, or a transplant constituent.

[Claim 74] The internal medicine according to claim 60 or the transplantation object for surgery which is a biological organization scaffold, the film, or a transplant constituent.

[Claim 75] The internal medicine according to claim 60 or the transplantation object for surgery which is a physic ingredient for blemishes, the film, or a transplant constituent.

[Claim 76] The internal medicine according to claim 60 or the transplantation object for surgery with which the liquid carrier ingredient of the nonaqueous solubility of a non-macromolecule exists in the amount of about 99.5 to 10 percentage by weight to the total weight of a constituent, the film, or a transplant constituent.

[Claim 77] The internal medicine according to claim 60 or the transplantation object for surgery with which the liquid carrier ingredient of the nonaqueous solubility of a non-macromolecule exists in the amount of about 99.5 to 25 percentage by weight to the total weight of a constituent, the film, or a transplant constituent.

[Claim 78] constituent in which the transplantation containing the following mixture for internal medicine or surgery or spraying is possible: liquid carrier ingredient [of the hyperviscosity of the nonaqueous solubility of a non-macromolecule which has the viscosity of 5000cP(s) at least at (a)37 degree C, and is not crystallized under a perimeter or physiological conditions in the flesh]; -- and -- (b) -- solvent; whose liquid carrier ingredient of the nonaqueous solubility of this non-macromolecule is fusibility

This mixture is 37 degrees C and has the viscosity of less than about 6,000 cPs here.

[Claim 79] The constituent in which the transplantation internal medicine according to claim 78 or for surgery which chooses a solvent from the group which consists of ethanol, dimethyl sulfoxide, ethyllactate, ethyl acetate, benzyl alcohol, a triacetin, 2-pyrrolidone, N-methyl pyrrolidone, propylene carbonate, Glico furol, and propellants for aerosol or spraying is possible.

[Claim 80] The constituent in which the transplantation internal medicine according to claim 78 or for surgery in which the solvent whose liquid carrier ingredient of the nonaqueous solubility of a non-macromolecule is fusibility exists in about 1 - 90% of the weight of the amount of the weight of the constituent in which transplantation or spraying is possible or spraying is possible.

[Claim 81] The constituent in which the transplantation internal medicine according to claim 80 or for surgery in which the solvent whose liquid carrier ingredient of the nonaqueous solubility of a non-macromolecule is fusibility exists in about 10 - 90% of the weight of the amount of the weight of the constituent in which transplantation or spraying is possible or spraying is possible.

[Claim 82] The constituent which mixture sprays [the transplantation internal medicine according to claim 60 or for surgery which has the viscosity of less than about 4,000 cPs at 37 degrees C or].

[Claim 83] The constituent which mixture sprays [the transplantation internal medicine according to claim 82 or for surgery which has the viscosity of less than about 1,000 cPs at 37 degrees C or].

[Claim 84] the approach of the Inn BIBO formation in the patient who needs it of a transplantation object, the film, or a transplant -- it is : It consists of the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1. mixture: (a) containing (1) following -- Solvent which the liquid carrier ingredient of the nonaqueous solubility of hyperviscous liquid carrier ingredient;, and (b) this non-macromolecule of the nonaqueous solubility which has the viscosity of 5,000cP(s) at least at 37 degrees

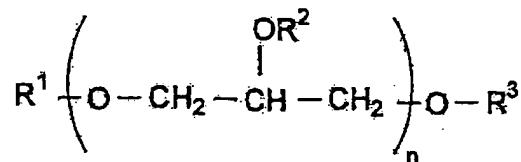
C, and is not crystallized under a perimeter or physiological conditions in the flesh dissolves; a patient's organization is contacted -- making -- this mixture -- 37 degrees C -- it is -- the viscosity of less than about 6000 cPs -- having --; and (2) -- the approach concerned of diffusing and including stripping or forming the transplantation object, film, or transplant of a liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule for this solvent in a patient's in-house by that cause.

[Claim 85] The approach according to claim 84 the aforementioned contact includes transplanting covering a vessel transplant with the aforementioned mixture, and this vessel transplant to a patient.

[Claim 86] An approach including the aforementioned contact injecting with or spraying the aforementioned mixture on the interior or the front face of an organization of a patient according to claim 84.

[Claim 87] The above-mentioned approach including contacting the liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility which is the medication method of the transplantation object for internal medicine or surgery , the film , or a transplant constituent , has the viscosity of 5,000cP(s) at least at 37 degrees C including the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 , and is not crystallize under a perimeter or physiological conditions in the flesh in the organization of the patient who needs it , and placing it .

[Claim 88] Compound:II which has the structure chosen from the group which consists of the following:
[Formula 14]



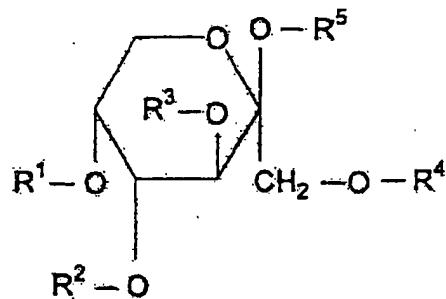
(R1, R2, and R3 are chosen from the group which consists of alkanoyl which has independently the alkanoyl which has hydrogen and two to 6 carbon, the alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and two to 6 carbon, and by which the acyloxy permutation was carried out among a formula, and n is 1-20, and at least one of R1, R2, and the R3 is except hydrogen);

III: [Formula 15]

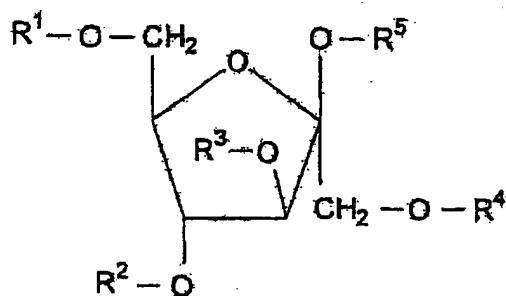


(n is the integer of 4-8 among a formula, and R1 and R2 are chosen from the group which consists of alkanoyl which has independently the alkanoyl which has hydrogen and two to 6 carbon, the alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and two to 6 carbon, and by which the acyloxy permutation was carried out, and at least one of R1 and the R2 is except hydrogen);

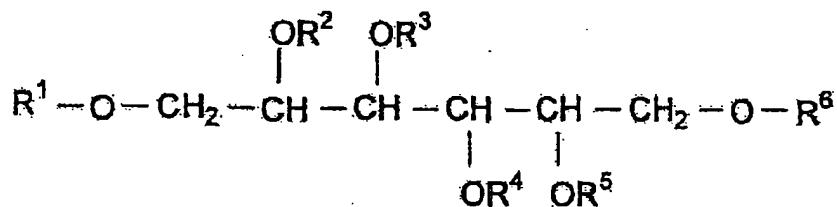
IV: [Formula 16]



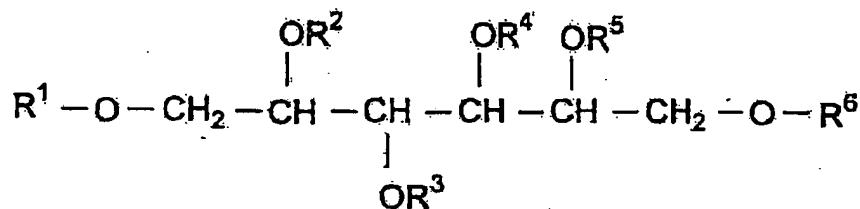
V: [Formula 17]



;
VI: (Choosing [and] R^1, R^2, R^3, R^4 , and R^5 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R^1, R^2, R^3, R^4 , and the R^5 is except hydrogen) [Formula 18]

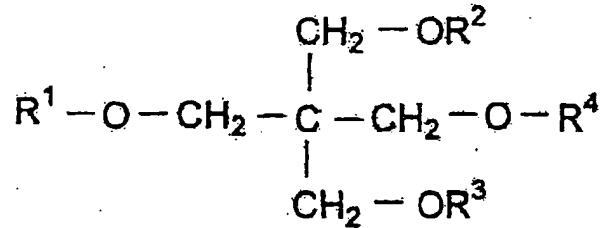


VII: [Formula 19]



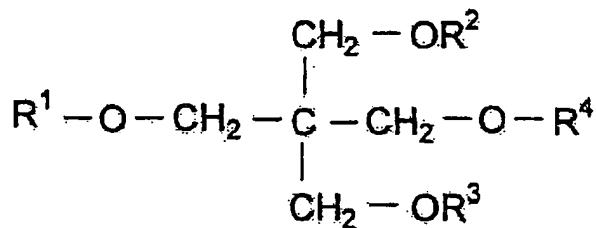
(R1, R2, R3, R4, R5, and R6 among a formula) The alkanoyl which has hydrogen and two to 6 carbon independently, the alkanoyl which has two to 6 carbon and by which the hydroxy permutation was carried out, And it chooses from the group which consists of alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out, and at least one of R1, R2, R3, R4, R5, and the R6 is except hydrogen.;

VIII: [Formula 20]



(Choosing [and] R1, R2, R3, and R4 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R1, R2, R3, and the R4 is except hydrogen).

[Claim 89] The compound according to claim 88 which has the following structure: [Formula 21]



(Choosing [and] R1, R2, R3, and R4 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R1, R2, R3, and the R4 is except hydrogen).

[Translation done.]

* NOTICES *

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1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

Field of background 1. invention of invention This invention is related to the new non-high molecular compound and new constituent which form the hyperviscous ingredient of the liquid suitable for the use as a device for internal medicine or surgery in the controlled format in the delivery list of the activity matter biologically. These ingredients can be diluted with a solvent, can make the ingredient of hypoviscosity able to form further suitably, and can make administration of this ingredient easy. This solvent may be water-insoluble nature, or may be water solubility, from this ingredient, a water soluble solvent is Inn BIBO, and it is spread promptly, or it moves and it leaves a hyperviscous liquid ingredient further.

[0002]

2. Explanation of related technique Wide range research has been made in the field of the system for the emission by which the biodegradable physiological active substance was controlled. Since the biodegradability matrix for drug delivery does not need to remove the device in which the drug carried out depletion, it is useful.

[0003]

The most common matrix ingredients for drug delivery are polymeric materials. For the field of a biodegradability macromolecule, composition and the biodegradability of polylactic acid are in 1966. Since it was reported by Kulkarni etc. ("Polylactic acid for surgical implants" Arch.Surg., 93:839), it has developed quickly. The polymer of the Pori anhydride, polyester, for example, poly glycolide, and a poly lactide-KOGURI corridor, polyamino acid, for example, the poly lysine, polyethylene oxide, and acrylic termination polyethylene oxide and a copolymer, a polyamide, polyurethane, poly ortho ester, a polyacrylonitrile, and polyphosphazene are contained in the example of other polymers reported useful as a matrix for the device for delivery. For example, please refer to No. 4,530,840 (the poly lactide, poly glycolide, and copolymer), such as U.S. Pat. No. 4,891,225 of Langer and No. 4,906,474 (Pori anhydride), No. 4,767,628 of Hutchinson (poly lactide and poly lactide-KOGURI corridor acid), and Tice, and No. 5,234,520 (biodegradable polymers for controlled delivery in treating periodontal disease, such as Dunn).

[0004]

The resolvability ingredient of the living thing origin is common knowledge, for example, the gelatin over which the bridge was constructed is contained. The bridge was constructed over hyaluronic acid as a bloating tendency polymer of the resolvability for biomedical application, and it has been used (U.S. Pat. No. 4,957,744, such as Della Valle; (1991) "Surface modification of polymeric biomaterials for reduced thrombogenicity" Polym.Mater.Sci.Eng., 62:731-735].

[0005]

The biodegradability hydrogel was also developed biologically because of the use in the controlled drug delivery as a carrier of the activity matter (for example, hormone, an enzyme, an antibiotic, an anti-neoplasm agent, and cell suspension). The controlled emission to a local organization or systemic

circulation of those kinds was attained by temporary preservation list of the functional property of the kind carried. For example, please refer to U.S. Pat. No. 5,149,543 of Cohen. The film which has the permeability, the pore dimension, and catabolic rate of a certain range which was suitable for various application in surgery, medical diagnosis, and a therapy with suitable selection of hydrogel macromere is generable.

[0006]

Many dispersed systems are used as a carrier of current and the matter (especially biologically activity compound), or are investigated for use. The dispersed system used for physic and the compound for makeup can be classified in suspension or a milky lotion. Suspension is defined as a solid particulate of the dimension range of hundreds of microns from several nanometers distributed in the liquid medium which uses a suspending agent. A microsphere, a microcapsule, and NANOSU fair are included in a solid particulate. The liquid of 1 distributes in other liquids and a milky lotion is defined as what was stabilized with an emulsifier, for example, a surfactant, and the interface film of a lipid. Oil Nakamizu and a water middle oil milky lotion, a multiplex milky lotion, a micro emulsion, a minute drop, and liposome are contained in a milky lotion compound. A minute drop is a single lamellae phospholipid vesicle which consists of a spherical lipid layer which has an oil phase inside, as U.S. Pat. No. 4,622,219 published by Haynes and No. 4,725,442 were defined. Liposome is a phospholipid vesicle manufactured by mixing the polar lipid of water-insoluble nature with a water solution. The entropy which is produced by mixing an underwater and insoluble lipid and which is not desirable produces a regular assembly in the altitude of the film which this alignment of the phospholipid which has the shut-up water solution closed.

[0007]

U.S. Pat. No. 4,938,763, such as Dunn, dissolves the thermoplastic polymer of water-insoluble nature of non-reactivity in the water-soluble solvent of biocompatibility, forms a liquid, arranges the liquid inside of the body, and is indicating the formation approach in Inn SHITU of the transplantation object by carrying out stripping of this solvent and generating a solid transplantation object. This polymer solution can be arranged inside of the body with a syringe. This transplantation object can take the configuration of the opening of that perimeter. In another example, this transplantation object is formed excluding a solvent from the low-grade polymer polymer of a liquid of the reactivity (addition of a curing catalyst is usually used) which hardens in a proper place and forms a solid-state.

[0008]

Although many ingredients have been evaluated per [in delivery of the controlled matter] use, the demand to giving the still easier system of low toxicity for this delivery is continuing existing. For example, the above-mentioned delivery system needs preparation of a polymer and the polymer matrix with which it filled up, a hydrogel, or other complicated constituents with brittle **. There is a demand to the delivery system distribution of the liquid base which is easily blended with the matter which should be sent especially and is easily prescribed for the patient.

[0009]

So, it is the purpose of this invention to offer the easy system for delivery of the matter.

[0010]

It is other purposes of this invention to offer the delivery system of the liquid base which is easily blended with the matter which should be sent and is easily prescribed for the patient.

[0011]

It is other purposes of this invention to offer the approach of the delivery by which the matter in the system of the easy liquid base was controlled.

[0012]

Epitome of invention This invention is related to the usage as the vehicle, for example, a controlled vehicle for delivery, for matter (for example, physiological active substance) delivery of these compounds and a constituent at the constituent list containing a compound and them. This invention is related also to the usage as these compounds, constituents and those internal medicine, or a device for surgery (for example, the transplantation object for internal medicine or surgery, the film, or a transplant

constituent) again. Generally, these constituents are liquid gestalten and contain the liquid carrier ingredient (it is a perimeter, or in the flesh under physiological conditions, it does not crystallize (if it remains as it is)) of the hyperviscosity of the nonaqueous solubility of at least 1 which consists of the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 which has the viscosity of 5,000cP(s) at least at 37 degrees C. It can be made to be able to dissolve in the solvent which can be permitted physiologically, and these constituents can reduce viscosity, and can make administration easy. However, after administration of the constituent containing a water-soluble solvent, this solvent is diffused from this ingredient, or is diffused, so, viscosity increases intentionally and, thereby, the matrix for the emission by which it was controlled for the transplantation object for a physiological active substance, internal medicine, or surgery, the film, or a transplant is formed. Although a nonaqueous solubility solvent can also be used, it will be far spread slowly from non-macromolecule ester or mixed ester.

[0013]

The dissolution in a solvent is useful especially when using the non-macromolecule ester or the mixed ester which has very high viscosity (for example, being 37 degrees C 100,000 order of cP). although some the non-macromolecule ester or the mixed ester suitable for use by this invention has the viscosity which exceeds 5,000cP(s) at 37 degrees C -- so much -- viscosity -- not but, it can come out without it adds a solvent namely, -- as it is, and a medicine can be prescribed for the patient.

[0014]

The nonaqueous solubility which consists of the non-macromolecule ester or the mixed ester of the carboxylic acid of at least 1 with which this invention has the viscosity of 5,000cP(s) at least at 37 degrees C in other fields, It is related to the approach of medicating vegetation or an animal (Homo sapiens being included) with the activity matter biologically, by medicating vegetation or an animal with a hyperviscous liquid carrier ingredient (it not crystallizing under a perimeter or physiological conditions in the flesh) and the hyperviscous constituent which contains the activity matter biologically. a specific medication method can be changed and can include partial administration, internal use (as a solution and a milky lotion -- or a gelatine capsule), nose administration, lung administration, rectum administration, vagina administration or injection (in the case of an animal) and partial administration, or injection (in the case of vegetation).

[0015]

In other fields, this invention is related to the internal medicine containing the liquid carrier ingredient (in the flesh, it does not crystallize under a perimeter or physiological conditions) of the hyperviscosity of the nonaqueous solubility which consists of the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 which has the viscosity of 5,000cP(s) at least at 37 degrees C or the transplantation object for surgery, the film, or a transplant constituent.

[0016]

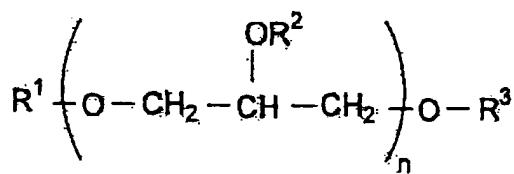
Furthermore, the transplantation object with which this invention contains the following in another field, the film, or a transplant, It is related to the formation approach in Inn BIBO in the patient who needs it. : The hyperviscosity of the nonaqueous solubility which consists of the non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 which has the viscosity of 5,000cP(s) at least at mixture:(a) 37 degree C containing (1) following, Solvent which the liquid carrier ingredient of the nonaqueous solubility of liquid carrier ingredient (it does not crystallize under perimeter or physiological conditions in the flesh); and a (b) non-macromolecule dissolves;

a patient's organization is contacted -- making (this mixture being 37 degrees C and having the viscosity of less than about 6000 cPs) --; and (2) -- this solvent -- a patient's in-house -- stripping -- or you make it spread and this forms the transplantation object, film, or transplant of a liquid carrier ingredient of the hyperviscosity of the nonaqueous solubility of a non-macromolecule. this invention -- still more -- alike -- a special field -- setting -- this mixture -- 37 degrees C -- it is -- less than about 4,000 cPs -- it has the viscosity of less than about 1,000 cPs much more specially.

[0017]

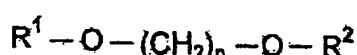
Furthermore, :II related to the new compound which has the structure which chooses this invention from

the group which consists of the following in another field: It is [Formula 22].



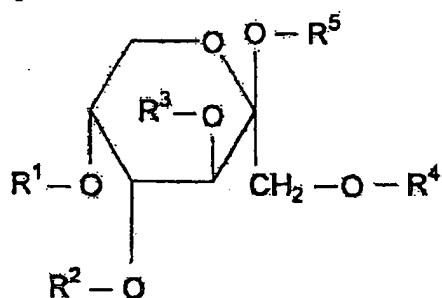
(R1, R2, and R3 are chosen from the group which consists of alkanoyl which has independently the alkanoyl which has hydrogen and two to 6 carbon, the alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and two to 6 carbon, and by which the acyloxy permutation was carried out among a formula, and n is 1-20, and at least one of R1, R2, and the R3 is except hydrogen);

III: [Formula 23]

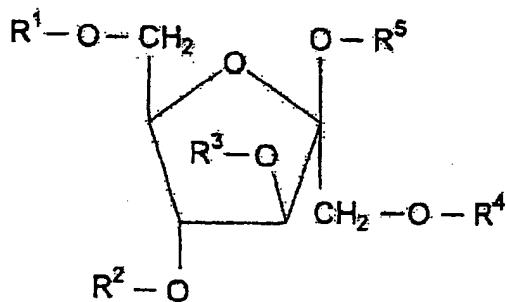


(n is the integer of 4-8 among a formula, and R1 and R2 are chosen from the group which consists of alkanoyl which has independently the alkanoyl which has hydrogen and two to 6 carbon, the alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and two to 6 carbon, and by which the acyloxy permutation was carried out, and at least one of R1 and the R2 is except hydrogen);

IV: [Formula 24]

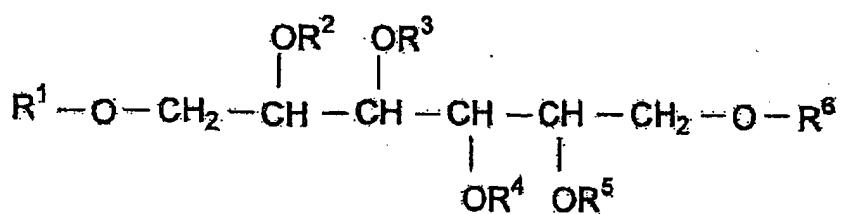


V: [Formula 25]

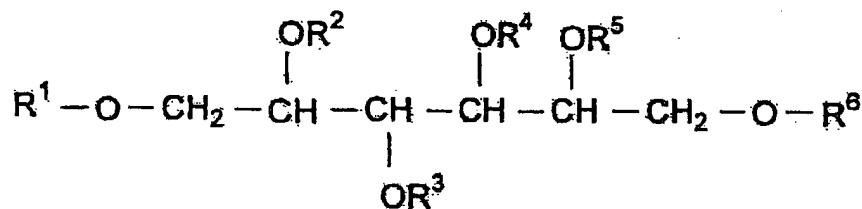


(Choosing [and] R1, R2, R3, R4, and R5 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R1, R2, R3, R4, and the R5 is except hydrogen);

VI: [Formula 26]

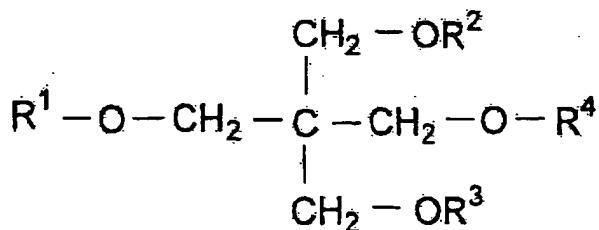


VII: [Formula 27]



(R1, R2, R3, R4, R5, and R6 among a formula) The alkanoyl which has hydrogen and two to 6 carbon independently, the alkanoyl which has two to 6 carbon and by which the hydroxy permutation was carried out, And it chooses from the group which consists of alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out, and at least one of R1, R2, R3, R4, R5, and the R6 is except hydrogen.;

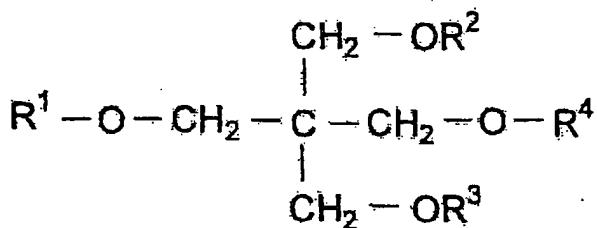
VIII: [Formula 28]



(Choosing [and] R1, R2, R3, and R4 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R1, R2, R3, and the R4 is except hydrogen).

[0018]

: in which this new compound has the following structure in a much more special field -- [Formula 29]



(Choosing [and] R1, R2, R3, and R4 from the group which consists of the alkanoyl which has hydrogen and two to 6 carbon, alkanoyl which has two to 6 carbon, and by which the hydroxy permutation was carried out, and alkanoyl which has two to 6 carbon, and by which the acyloxy permutation was carried out independently among a formula, at least one of R1, R2, R3, and the R4 is except hydrogen).

[0019]

The liquid constituent of this invention can be used in which use or application indicated by the United States patent application 08th / No. 944,022, No. 478,450, and No. 08/474,337 (present, U.S. Pat. No. 5,747,058) (it uses into this specification by considering all these contents of each as reference) about HVLCM or LVLCM.

[0020]

Liquid carrier ingredient of the hyperviscosity of the detailed explanation nonaqueous solubility of a specific example The hyperviscous liquid carrier ingredient (what is not crystallized under a perimeter or physiological conditions in the flesh) into which it is nonaqueous solubility and has the viscosity of 5,000cP(s) at least at 37 degrees C with a non-macromolecule (even in case of suitableness, at least 10,000, and 15,000;20,000;25,000cP or viscosity of 50,000cP(s)) should be chosen. The vocabulary "nonaqueous solubility" says the ingredient which dissolves in water to extent of less than 1 percentage by weight under ambient conditions. The vocabulary "a non-macromolecule" says the ester or the mixed ester to which a functionality unit has few acid parts (namely, oligomer) which are carrying out repeatedly [count] to the ester or the mixed ester list which does not have a repetitive unit into an acid part in essence. Although the ingredient which has many same adjoining repetitive units from five into the acid part of ester is generally removed from the vocabulary "a non-macromolecule" when using here,

the ingredient containing a dimer, a trimer, a tetramer, or a pentamer is contained in the range of this vocabulary. When ester is formed from the hydroxy content carboxylic-acid (for example, lactic-acid or glycolic acid) part which can further be esterified, the number of repetitive units is calculated based on the number of not the number of a lactic acid or glycolic-acid parts but a lactide, or glycolide parts (in a lactide repetitive unit, a glycolide repetitive unit contains two glycolic-acid parts esterified in the hydroxy **** carboxy part, respectively including two lactic-acid parts esterified in the hydroxy **** carboxy part, respectively). It is considered that the ester which has the etherification polyol of 1 - abbreviation 20 into an alcoholic part, or has the glycerol parts of 1 - abbreviation 10 is a non-macromolecule (when using this vocabulary here).

[0021]

In a specific example, when a hyperviscous liquid carrier ingredient (HVLCM) is mixed with the activity matter biologically for the delivery which was mixed with the solvent which forms the liquid carrier ingredient (LVLCM) of the hypoviscosity which can be prescribed for the patient as the transplantation object for internal medicine or surgery, a transplant, or film and which was controlled at the time [delivery], in the case of some of such combination, viscosity falls intentionally. Typically, since the receipts and payments to the transplantation manual stage of a syringe and others are still easier for the constituent of the matter [activity / target / LVLCM // biology], it is biologically easier to put [HVLCM /] on the inside of the body than the constituent of the activity matter. It can also make it easy to blend as a milky lotion. In addition, especially as for the viscosity range of LVLCM, less than about 4,000 cPs and less than about 1,000 cPs of less than about 6,000 cPs of things [less than 200 cPs / the Inn BIBO application] typically are found out much more especially much more especially.

[0022]

Specific HVLCM used by this invention may be at least one of the various ingredients. The non-macromolecule ester or the mixed ester of a carboxylic acid of at least 1 is contained in a suitable ingredient. In a specific example, this ester is formed from the polyol which has the hydroxy part of about 2-20, and the esterified carboxylic acid (the etherification polyol of 1 - abbreviation 20 can also be included). The carboxylic acid (for example, the thing obtained according to the ring breakage nature alcoholysis of lactone or annular carbonate or the thing obtained according to the alcoholysis of a carboxylic anhydride) which has the hydroxy group of at least 1 is contained in the carboxylic acid suitable for especially forming the acid part of the ester of HVLCM. Amino acid is also suitable for forming ester with polyol. In a specific example, this ester or mixed ester contains the alcoholic part which has the carboxylic acid of at least 1 obtained according to the alcoholysis of a carboxylic anhydride (for example, cyclic anhydride), and at least one esterified end hydroxy part.

[0023]

A glycolic acid, a lactic acid, an epsilon-hydroxy caproic acid and the lactone of arbitration or a lactam, trimethylene carbonate, and the dioxa non are contained in the nonrestrictive example of the suitable carboxylic acid in which it is esterified and deals so that HVLCM of this invention may be formed. These hydroxy content acids are further esterified by the reaction of these very thing, and its hydroxy part and further carboxylic acid (the same things as other carboxylic-acid parts in this ingredient may also differ), and it deals in them by it. Although glycolide, a lactide, epsilon-caprolactone, a butyrolactone, and a valerolactone are contained in suitable lactone, it does not restrict to these. Although trimethylene carbonate and propylene carbonate are contained in suitable carbonate, it does not restrict to these.

[0024]

The alcoholic part of this ester or mixed ester can be guided from the polyhydroxy alcohol which has about two to 20 hydroxy group, and can be formed according to etherification of 1 - 20 polyol molecule as mentioned above. What is guided by removing at least one hydrogen atom from :1 functionality C1 - C20 alcohol, bifunctional C 1 - C20 alcohol, trifunctional alcohol, a hydroxy content carboxylic acid, hydroxy content amino acid, phosphate content alcohol, tetrafunctional alcohol, sugar-alcohol, monosaccharide and disaccharide, saccharic acid, and polyether polyol is contained in a suitable, alcoholic part. Especially these alcoholic parts can contain at least one of a dodecanol, hexandiol

especially 1,6-hexanediol, glycerol, a glycolic acid, a lactic acid, hydroxybutyric acid, a hydroxy valeric acid, a hydroxy caproic acid, a serine, ATP, a pentaerythritol, a mannitol, a sorbitol, a glucose, a fructose, shoe cloth, glucuronic acid, the poly glycerol ether (1-glycerol unit content of about 10), and the polyethylene glycols (1-ethylene glycol unit content of about 20).

[0025]

In the specific example of this invention, the carboxylic-acid part of at least 1 of the ester of this invention or mixed ester contains the oxy-part of at least 1. Furthermore, in a much more specific example, each of these carboxylic-acid parts contains the oxy-part of at least 1.

[0026]

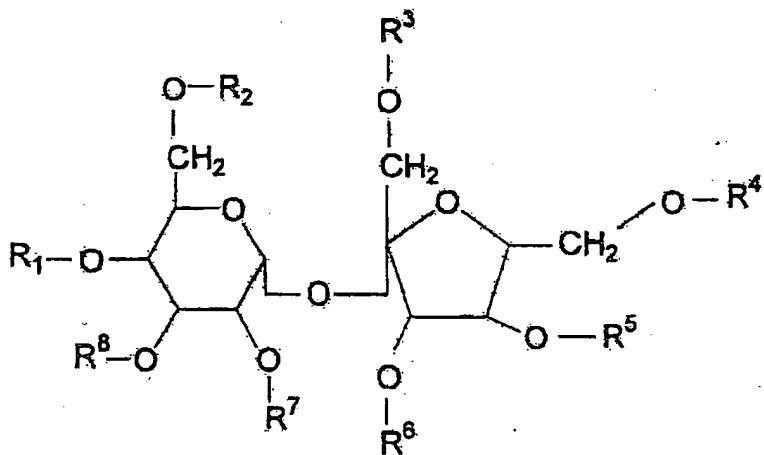
In other specific examples, the carboxylic-acid part of at least 1 of the ester of this invention or mixed ester contains 2 - 4 carbon atom. In a much more specific example, each of the carboxylic-acid part of the ester of this invention or mixed ester contains 2 - 4 carbon atom.

[0027]

In other much more specific examples of this invention, the carboxylic-acid part of at least 1 of the ester of this invention or mixed ester has 2 - 4 carbon atom, and contains the oxy-part of at least 1. In other much more specific examples of this invention, each of the carboxylic-acid part of the ester of this invention or mixed ester has 2 - 4 carbon atom, and contains the oxy-part of at least 1.

[0028]

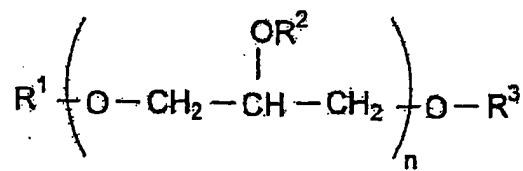
:I which has the structure which chooses this invention from the group which HVLCM becomes from the following in that case in a specific example including a compound, an above-mentioned constituent, and the above-mentioned usage: It is [Formula 30].



(R1, R2, R3, R4, R5, R6, R7, and R8 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula);

(At least three, R1, R2, R3, R4, R5, R6, R7, and R8, among a formula) it is except hydrogen --; and (R1, R2, R3, R4, R5, R6, R7, and R8 are chosen from the group which consists of acetyl and isobutyryl among a formula, and at least three, R1, R2, R3, R4, R5, R6, R7, and R8, are acetyl);

II: [Formula 31]



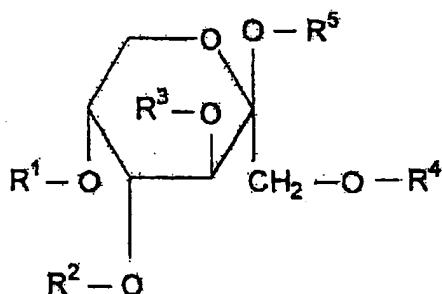
(Choosing independently R1, R2, and R3 from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula, n is 1-20);

III: [Formula 32]

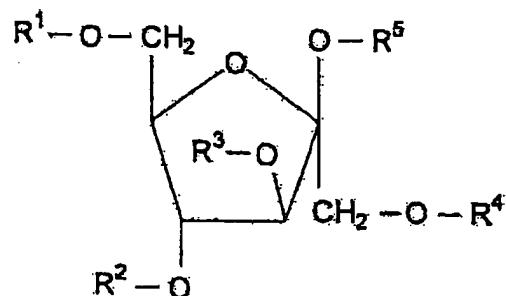


(n is the integer of 4-8 among a formula, and R1 and R2 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out);

IV: [Formula 33]

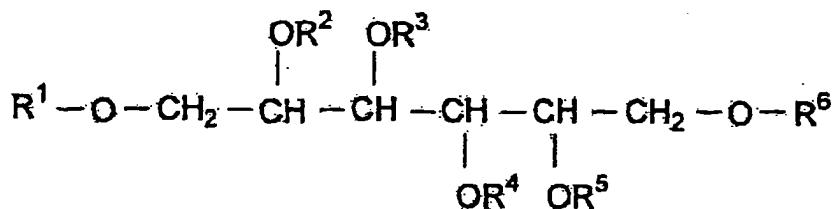


V: [Formula 34]

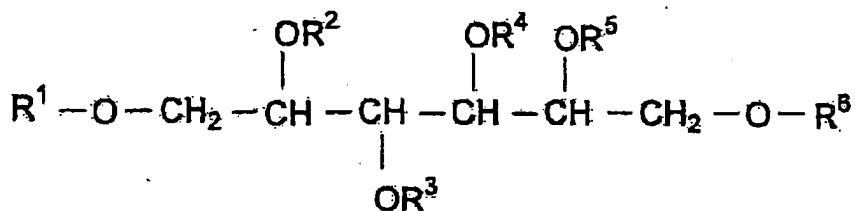


(R1, R2, R3, R4, and R5 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among Formula IV and V);

VI: [Formula 35]

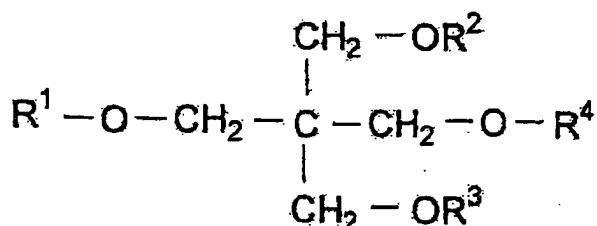


VII: [Formula 36]



(R1, R2, R3, R4, R5, and R6 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among Formulas VI and VII);

VIII: [Formula 37]



(R1, R2, R3, and R4 are independently chosen from the group which consists of hydrogen, alkanoyl, alkanoyl by which the hydroxy permutation was carried out, and alkanoyl by which the acyloxy permutation was carried out among a formula).

[0029]

In each of formula I-VIII, at least one of the alkanoyl radicals by which the acyloxy permutation of alkanoyl and the alkanoyl **** by which the hydroxy permutation was carried out was carried out may contain the alkanoyl part which has 2 - 6 carbon atom (carbonyl carbon is included). Moreover, in other much more specific examples of this invention, each of formula I-VIII contains at least one alkanoyl part by which the hydroxy permutation was carried out or the acyloxy permutation was carried out. Furthermore, in a much more specific example, at least one of the alkanoyl parts of these by which the hydroxy permutation was carried out or the acyloxy permutation was carried out contains the alkanoyl part which has 2 - 6 carbon atom (carbonyl carbon is included).

[0030]

The acyl group which forms the acyloxy substituent of this invention may be the part of the arbitration

originating in a carboxylic acid according to the terminological "acyl" definition generally accepted. Especially the acyl group of the constituent of this invention may be the thing (R9 is the alkyl by which the oxy-permutation of 2-6 was carried out suitably) of an R9CO-mold. This oxy-permutation can take the gestalt of a hydroxy permutation or the permutation of the further acyl part. For example, R9 may be the oligomer (what was combined by the ester bond between HIDOROKISHI of the acid of 1, and the carboxy of other acids) of the carboxylic acid by which the oxy-permutation was carried out. In a much more specific example, R9 is the lactide or glycolide unit of 1-5 (in a lactide unit, a glycolide unit contains two glycolic-acid parts esterified together including two lactic-acid parts esterified together). Or R9 can contain a mixed lactide and a glycolide unit, or it can contain a mixed lactic acid and a glycolic acid (when a lactide or a glycolide unit does not exist).

[0031]

The compound according to Formula II or III is contained in a specific HVLCM ingredient (R1, R2, and R3 are lactoyl, the poly lactoyl, epsilon-caproyl, hydroxy acetyl, or polyhydroxy acetyl independently among a formula, and they are the poly lactoyl and epsilon-caproyl or the poly lactoyl, and polyhydroxy acetyl).

[0032]

Use of the comparatively small chain (2 - 6 carbon atom) in the ester or the mixed ester of this invention and the carboxylic-acid part by which the oxy-permutation was carried out is advantageous. When these acid parts exist with the gestalt of oligomer ester (namely, acid part of the consecutiveness combined with the front acid part by esterification of consecutive carboxy and front OKISHI), since hydrolysis of this ingredient is a hydrophilic property much more, it is quite easier than the oligomer made from more carbon atoms than 6. Generally, for drug delivery, although HVLCM is water-insoluble nature, it is desirable that it is a hydrophilic property partly. Generally, HVLCM further compounded using the unit (it measures by the still higher O:C ratio) of a hydrophilic property absorbing water still more quickly, and decomposing much more quickly is expected. For example, HVLCM generated by carrying out covalent bond of the four-mol glycolide to one-mol glycerol absorbing water much more quickly than HVLCM generated by carrying out covalent bond of two mols glycolide and the two-mol lactide to one-mol glycerol, and decomposing much more quickly is expected. The same increment is expected about a much more flexible molecule and the spherical molecule based on a free volume argument which branched one layer. Flexibility and the use of a molecule which branched may also have the profits to which the viscosity of LVLCM is reduced. Use of the carboxylic acid which has use and the oxy-permutation of different chain length's carboxylic acid and/or polyol gives exact control of the hydrophilic property of the generated ester, and extent of solubility. or [following these ingredients on the emission and it to the inside of the body of a physiological active substance which were controlled] -- or it is fully resistance at decomposition by Inn BIBO as hydrolysis of oxy-association by continuing Inn BIBO can be given.

[0033]

Furthermore, in a much more specific example, this invention eliminates the acetate and iso butyrate ester of shoe cloth which have a ratio to the iso butyrate acid part of the acetate of 2:6. However, shoe cloth acetate ISOBUCHIRETO which has a ratio to the iso butyrate part of the acetate of 2:6 is contained within the limits of this invention (it indicates and illustrates below) for delivery of a lysozyme, rip-off TAKIZERU, 5-fluorouracil, and anti-retrovirus agents (AZT, ddC, etc.) in the list for the use in an aerosol compound. This ingredient can be manufactured according to the procedure indicated by U.S. Pat. No. 2,931,802.

[0034]

Generally, the HVLCM ester of this invention can be manufactured by making it react with the carboxylic acid of at least 1 which forms the acid part of the ester which generated the alcohol (especially polyol of at least 1) of at least 1 which forms the alcoholic part of the generated ester, lactone, a lactam, carbonate, or a carboxylic anhydride. In some cases, addition of strong acid or a strong base esterification catalyst is used, but an esterification reaction can be easily performed by heating. Or the esterification catalyst of 2-ethyl hexanoic acid, for example, the first tin, can be used. It heats stirring

the heated reaction mixture (or whether it is accompanied by the catalyst, thing by which it is not accompanied), and subsequently, it dries for example, in a vacuum, any unreacted start ingredients are removed, and the product of a liquid is generated. Shoe cloth acetate ISOBUCHIRETO can be manufactured according to the procedure of a publication to U.S. Pat. No. 2,931,802.

[0035]

About this, polyol can be regarded as the initiator of oligomerization in the semantics of a carboxylic acid of giving the substrate of esterification of the oligomer of a lactide, glycolide, or other esterification hydroxy permutation carboxylic acids especially.

[0036]

Solvent As mentioned above, in one example of this invention, HVLCM is mixed with a viscosity-down solvent and the liquid carrier ingredient (LVLCM) of still lower viscosity is formed, and subsequently, after mixing with the matter [activity / target / which should be sent / biology], a medicine can be prescribed for the patient. These solvents may be the things of a water-soluble nonaqueous solubility or a water-soluble water miscibility. An acetone, benzyl alcohol, benzyl benzoate, N-(beta hydronium methyl) RAKUTAMIDO, A butylene glycol, a caprolactam, a caprolactone, corn oil, DESHIRU methyl sulfoxide, wood ether, dimethyl sulfoxide, 1-dodecylazacycloheptane-2-one, ethanol, ethyl acetate, Ethyllactate, ethyl oleate, glycerol, the Glico furol (tetra-glycol), The isopropyl myristate, methyl acetate, a methyl ethyl ketone, a N-methyl-2-pyrrolidone and MIGLYOL (a caprylic acid and/or a capric acid, glycerol, or ester with alkylene glycol --) For example, MIGLYOL810 or 812 (a caprylic acid / capric-acid triglyceride), MIGLYOL818 (a caprylic acid / capric acid / linolic acid triglyceride), MIGLYOL829 (a caprylic acid / capric acid / succinic-acid triglyceride), MIGLYOL840 (propylene glycol dicaprylate / KAPURETO), Oleic acid, peanut oil, a polyethylene glycol, propylene carbonate, 2-pyrrolidone, sesame oil, SOLKETAL ([**] -2, the 2-dimethyl -1, 3-dioxolane-4-methanol), A tetrahydrofuran, TRANSCUTOL (diethylene glycol monoethyl ether, carbitol), a triacetin, triethyl SHITORETO, and these combination are included, and it gets. Supposing it should apply it, using this constituent as aerosol (for example, local application sake), in addition, a solvent The propellants (for example, trichlorofluoromethane and fluoro carbon 21), for example, CFC propellants, of at least 1, It is non-CFC propellants (for example, tetrafluoro ethane (R-134a), 1, 1, 1, 2, 3 and 3, 3-heptafluoro propane (R-227), wood ether, a propane, and butane), or this ** can be contained. Benzyl benzoate, dimethyl sulfoxide, ethanol, ethyllactate, glycerol, the Glico furol (tetra-glycol), a N-methyl-2-pyrrolidone, MIGLYOL810, a polyethylene glycol, propylene carbonate, 2-pyrrolidone, and tetrafluoro ethane are contained especially in suitable solvent and/or propellants.

[0037]

When using this constituent as LVLCM in relation with administration of the activity matter biologically, it should contain the solvent with which HVLCM serves as fusibility. The matter which should be prescribed for the patient in a certain case is also fusibility in this solvent. This solvent should be avirulent or biocompatibility. A toxic solvent should not be used for medicine or the agricultural purpose. The solvent used in order to inject an animal with this constituent should not be caused except for the case where it is the effectiveness of a request of a significant organization stimulus or a significant necrosis of a stimulus or a necrosis, by the transplantation part.

[0038]

In one example, this solvent should be water solubility at least, as it is quickly spread by body fluid or other aquosity environments and is made to make solidify a constituent or solidify. The increments in the viscosity to which it sets in other examples, and this solvent spreads and corresponds from a constituent are not completely water or body fluid, and a miscibility so that it may become late.

[0039]

When using 1,6-hexanediol or the ester of glycerol as HVLCM, some possible solvents are ethanol, N-methyl pyrrolidone, propylene carbonate, and PEG400.

[0040]

Typically, this solvent is added to these constituents to the total weight of this constituent in the amount of about one to 95 percentage by weight, especially the range of about five to 90 wt%. In addition, much

more especially this solvent exists in this constituent in the amount of the range of about ten to 55 percentage by weight. In other specific range, about ten to 50 percentage by weight and about ten to 30 percentage by weight are contained.

[0041]

When it combines with HVLCM independently, or when it combines with the solvent for HVLCM, the further example includes use of the solvent which is not a solvent for HVLCM so that the generated constituent may not form a milky lotion. As for this milky lotion, in the case of the SAIB/MIGLYOL mixture emulsified underwater or in glycerol etc. can contain HVLCM in a dispersed phase, or they can contain HVLCM as a continuous phase component (in the case of the water solution emulsified in HVLCM, or the solution of HVLCM in a water miscibility solvent etc.).

[0042]

Matter which should be sent When using HVLCM or LVLCM as a vehicle for the emission by which the matter to an animal or vegetation was sent or controlled, this matter may be matter of arbitration in which a desired property is shown. In a specific example, this matter is activity matter biologically.

[0043]

The vocabulary "it is the activity matter biologically" is an animal (although the mammals including birds and Homo sapiens are included), when using here. The drug which causes biological effectiveness when a medicine is prescribed for the patient for not restricting to these, A peptide, protein, a carbohydrate (monosaccharide, oligosaccharide, and polysaccharide are included), The polypeptide and protein of a nucleoprotein, mucoprotein, lipid protein, and composition, Or the small molecule combined with protein, a glycoprotein, a steroid, a nucleic acid (DNA, RNA, or these fragments of a gestalt of the arbitration containing CDNA), Inorganic or an organic molecule including a nucleotide, a nucleoside, an oligonucleotide (an antisense oligonucleotide is included), a gene, a lipid, hormone, vitamins (vitamin C and vitamin E are included), or these combination is said.

[0044]

Although human growth hormone, fibroblast growth factor (FGF), erythropoietin (EPO), platelet derived growth factor (PDGF), granulocyte colony-stimulating factor (g-CSF), cow somatotropin (BST), tumor necrosis factor (TNF), and transforming growth factor beta (TGF-beta), interleukin, an insulin, and interferon are contained in suitable protein, it does not restrict to these.

[0045]

When using a vocabulary drug here, internal use or the matter of arbitration applied externally is said as physic for illness or the therapy of a failure, recovery, or prevention. An immunosuppressant, an anti-oxidant, a narcotic, a painkiller, a chemotherapeutic drug, a steroid (a retinoid is included), Although hormone, an antibiotic, an antivirotic, an antifungal, a growth inhibitor, an antihistamine, an anticoagulant, an anti-light aging agent, a MERANOTORO pick peptide, a non-steroid and a steroid anti-inflammatory compound, an antipsychotic drug, and a radiation absorbent (UV absorbent is included) are included, it does not restrict to these.

[0046]

The matter [activity / target / vocabulary biology] also includes drugs, such as an insecticide, agricultural chemicals, a fungicide, a rodenticide, a vegetable nutrient, and a growth promotor.

[0047]

In one example, this constituent functions as a vaccine and the matter which should be sent is an antigen. This antigen may originate in a cell, bacteria, virions, or these protein. Like a convention here, antigens may be the ** protein which lures out an immunogenicity response in an animal, for example, mammalian, birds, or fishes, a peptide, polysaccharide, a glycoprotein, a glycolipid, nucleic acids, or these combination. Like a convention here, an immunogenicity response may be acidity or alkalinity, or may be cell medium nature. When antigenic is scarce, a standard covalent-bond technique (one [for example,] of the reagent kits of some marketing) can be used, and it can be combined with the ingredient with which an immunogenicity response is desired at a carrier or haptens, such as albumin.

[0048]

Virus protein, for example, influenza protein, human immunodeficiency virus (HIV) protein and A and

B or hepatitis C protein and bacteria protein, lipopolysaccharide, for example, a gram-negative bacterial cell wall, *Neisseria gonorrhoeae* protein, and a parvovirus are contained in the example of a suitable antigen. ***** lured out by prescribing a medicine for the patient with the vaccine which mediates a mucosal surface with HVLCM (the solvent for reducing viscosity as mentioned above suitably is used) of this invention from a nose, a vagina, or the rectum with an immunogenicity ingredient can also perform both membrane and a generalized immune response using the constituent of this invention. This immunogenicity ingredient may be immunogenicity drugs of arbitration with which delivery in membrane tissue is desired. These immunogenicity ingredients contain the antigen for carrying out a vaccination to the antigen for carrying out a vaccination to the disease caused, the antigen and macroscopic living thing, for example, the helminthiasis original object, for carrying out a vaccination to a virus, bacteria, protozoa, or a fungal disease (for example, disease caused by respiratory syncytium, parainfluenza viruses, a *Hemophilus influenzae*, *Bordetella pertussis*, *Neisseria gonorrhoeae*, the *Streptococcus pneumoniae* and the *Plasmodium falciparum*, or other pathogenic microorganisms), and allergen. HVLCM or LVLCM is chosen from above-mentioned formula II-VIII in the further much more special field of this example. This type of vaccine can be prepared and prescribed for the patient in 132,096 (April 30, 1999 application) according to the procedure indicated per SAIB the 60th of U.S. temporary application (it uses into this specification by considering all the contents of this application as reference).

[0049]

In other examples, this constituent functions as a constituent for emission by which it was controlled for the playback therapy in *Homo sapiens* and an animal. For example, HVLCM or LVLCM is combinable with gonadotropin releasing hormone, its analog, or agonist. In the special field of this example, HVLCM or LVLCM is not SAIB which has the acetate pair butyrate ratio 2:6. HVLCM or LVLCM is chosen from above-mentioned formula II-VIII in the still much more special field of this example. These constituents can be prepared and prescribed for the patient according to the procedure indicated by the U.S. application 09th / 123 (December 30, 1997 application) about SAIB (all the contents of this application are used into this specification as reference). [001 and 123]

[0050]

For the nonrestrictive example of a pharmacology-ingredient, an anti-infective agent, for example, nitrofurazone, sodium propionate and an antibiotic (penicillin and a tetracycline --) Oxytetracycline, chlorotetracycline, bacitracin, Nystatin, streptomycin, a neomycin, a polymyxin, gramicidin, a chloramphenicol, an erythromycin, and azithromycin are included --; sulfonamide (sulfacetamide --) Sulfamethizole, the sulfamethazine, a sulfamerazine, and sulfisoxazole are included. And an antivirotic (idoxuridine is included); An antiallergic agent, for example, antazoline, A meta-pilus ten, chlorpheniramine, mepyramine PUROFEMPIRIDAMIN, Hydrocortisone, cortisone, hydrocortisone acetate, dexamethasone 21-phosphate, Fluocinolone, triamcinolone, the medrysone, prednisolone, Pre boss ZORON 21-sodium succinate and prednisolone acetate; A hyposensitization agent, for example, a ragweed pollen antigen, The dry grass pollen antigen, a dust antigen, and a milk antigen; A vaccine, for example, variola, yellow fever, Distemper, hog cholera, varicella, anti-poison, scarlet fever, a diphtheria toxin, a tetanus toxin, ****, pertussis, influenza rabies, the mumps, measles, poliomyelitis, and a Newcastle disease vaccine; A congestion remover, for example, phenylephrine, Naphazoline and tetrahydrazo phosphorus; A miotic and anticholinesterase, for example, pilocarpine, ESUPE phosphorus salicylate, carbachol, diisopropyl fluoro phosphate, Phospholine iodide and demecarium bromide; A parasympathetic nerve cutoff agent, for example, atropine sulfate, Cyclopentolate, homatropine, scopolamine, tropicamide, eucatropine and hydroxyamphetamine; -- sympathomimetic agent, for example, epinephrine,; -- a sedative and a hypnotic, for example, pentobarbital sodium, -- Phenobarbital, secobarbital sodium, codeine, a urea (a-BUROMO iso valeryl), carbromal; -- psychic energizer, for example, 3-(2-aminopropyl) Indore acetate, and 3-(2-amino butyl) Indore acetate; -- a tranquilizer, for example, reserpine, -- chlorpromazine and thiopropazate; -- anesthetic, for example, NOBIKAIN, and bupivacaine; -- androgen nature steroid, for example, methylthioadenosine, and full ORIME sterone; -- estrogen, for example, estrone, -- 17-fl-estradiol, ethinylestradiol, and a diethylstilbestrol; A

progesterone agent, for example, progesterone, Megestrol, meringue SUTORORU, and KURORU serious non, the ethisterone, The norethynodrel, 19-norprogesterone, the norethindrone, Medroxyprogesterone and 17-O-hydroxy-progesterone; A humoral agent, PGE2 and PGF2, for example, a prostagladin, and a PGF2; antipyretic, for example, aspirin, [for example,] Sodium salicylate and salicylamide; Antispasmodic, for example, atropine, Methantheline, papaverine, and methscopolamine bromide; Antimalarial, for example, 4-amino quinoline, 8-amino quinoline, a chloro kinin and the pyrimethamine, and an antihistamine, for example, diphenhydramine, The dimenthidrinate, a TORIPEREN amine, perphenazine, and chloro phenazine; A cardioactive agent, for example, JIBENZU hydroflumethiazide, Flumethiazide, chlorothiazide, and amino TORETO; the bioactive peptide and protein (a growth factor, a cell adhesion factor, cytokine, and a biological response modifier are included) of a nutrient, for example, a vitamin, nature, and composition are contained.

[0051]

An activity compound is contained in sufficient amount to send an amount effective in attaining desired effectiveness for a host animal or vegetation to this constituent. It depends on a desired emission profile, the concentration of a drug required for biological effectiveness, and the request period of drug release for the amount of drugs [activity / target / which is built into this constituent / the drug or biology target].

[0052]

It depends for the concentration of a compound [activity / in this constituent] also on a factor well-known to other contractors of these again at absorption of a drug, inactivation, and an elimination rate list. The value of dosage should be noticed about changing also with the weight of the condition of disease which should be mitigated. It should be understood further that it is not what the specific patient of arbitration and a specific medication method of curing being adjusted with time according to decision of the expert who manages each need and the administration person of a constituent, or this administration, and the density range shown here are mere examples, and means restricting the range of a constituent or operation currently charged. This constituent can also be prescribed for the patient with 1 time of dosage, and can also be divided into some still smaller doses for changing and prescribing spacing for the patient.

[0053]

this -- biological -- the activity matter -- typical -- the inside of a constituent -- about 0.1 to 20 percentage by weight of the total weight of this constituent -- much more especially, it exists in the range of about 0.5 to 20 percentage by weight, and exists in about 1-15 or more percentage by weight much more typically. Other suitable range is about two to 10 percentage by weight. About very activity drugs, such as a growth factor, an optimum range is less than 1 % of the weight, and it is less than 0.0001%.

[0054]

Both matter of fusibility and insoluble matter can be distributed into HVLCM or LVLCM for the controlled delivery. Moreover, these compounds that contain the activity matter and HVLCM, or LVLCM biologically can offer the matrix for drug delivery which has further the property which blended with the excipient of a macromolecule and was changed. the constituent generated as a result -- a technique well-known for the time being in the fields -- a microsphere -- or it can form in the geometrical configuration and dimension of a macroscopic transplantation object and macroscopic others. Or the microsphere or transplantation object which incorporated the activity matter inside biologically and which preformed can be set by HVLCM as for example, a vehicle for injection, or LVLCM. HVLCM or LVLCM forms a secondary barrier and gives the drug delivery which increased here. According to a specific biological demand, this HVLCM or a LVLCM phase can also contain the activity matter biologically [others], and does not need to contain it. these -- others -- although activity matter may be any of the above-mentioned thing, the activity matter must fit inclusion in the microsphere or transplantation object by the well-known technique for the time being biologically in the fields.

[0055]

Additive Suitably, it can add to HVLCM or LVLCM, various additives can be changed like a request of the property of this ingredient, and the emission characteristic about the matter [activity / target / which this constituent contains especially / biology] can be changed. These additives may exist in the amount of sufficient arbitration to give a desired property to a constituent. Generally, the amounts of the additive to be used are the property of the additive, and the function of effectiveness which should be attained, and the work as a mold, however those who are not can determine them easily. The suitable additive is indicated by U.S. Pat. No. 5,747,058 (it uses into this specification by considering all the contents as reference). Water, a biodegradability polymer, the polymer that is not biodegradability, natural oil, synthetic oil, a carbohydrate or a carbohydrate derivative, mineral, BSA (bovine serum albumin), a surfactant, an organic compound, for example, a saccharide, and organic salt, for example, sodium SHITORETO, are included much more especially in a suitable additive. Some of additives of these classes are further explained to a detail below. Generally, it is made late compared with the same constituent which does not have an additive for the emission rate of the matter, so that an additive is not water solubility (namely, degree which is oleophilic). In addition, probably, it will be desirable to include the additive which increases properties, such as reinforcement of a constituent or porosity.

[0056]

Using addition of an additive, delivery time amount of an active ingredient can be lengthened and a constituent can also be made into what was suitable for prolonged administration at the failure or the sick therapy of responsibility. About this, what was indicated by U.S. Pat. No. 5,747,058 is contained in a suitable additive. The additive, for example, the cellulose system polymer, and biodegradability polymer of a macromolecule are contained especially in the additive suitable for this purpose. Cellulose acetate, cellulose ether, and cellulose acetate butylate are contained in a suitable cellulose system polymer. The poly acetone, the Pori anhydride and poly ortho ester especially polylactic acid, polyglycolic acid, the poly caprolactones, and these copolymers are contained in a suitable biodegradability polymer.

[0057]

the case where it exists -- an additive -- typical -- the inside of these constituents -- the total weight of a constituent -- receiving -- about 0.01 to 20 percentage by weight -- much more -- especially -- the amount of about 0.1 to 20 percentage by weight -- existing -- much more -- typical -- the inside of a constituent -- about 1, 2, or 5- it exists in the amount of about 10 percentage by weight. In a constituent, it is only little, a certain kind of an additive, for example, a buffer, and it exists.

[0058]

The following category is the nonrestrictive example of the class of the additive which can be used in this constituent.

[0059]

If having indicated here and the purpose to attain are given, easily, this contractor can choose other additives and can attain the desired purpose. It is thought that all these examples go into the inside of this indicated invention.

[0060]

A. Biodegradability polymer One category of an additive is a biodegradable polymer and oligomer. The emission profile of the matter which should be sent can be changed using these polymers, and integrity can be added to a constituent, or the property of a constituent can be changed. For the nonrestrictive example of a suitable biodegradability polymer and oligomer Pori (lactide), Pori (lactide-KOGURI corridor), Pori (glycolide), Pori (caprolactone), a polyamide, the Pori anhydride, polyamino acid, Poly ortho ester, poly cyanoacrylate, Pori (phosphogin), Non [Pori (phospho ester), polyester amide, and poly dioxa] Polyacetal, the poly ketal, a polycarbonate, poly alt.carbonate, Resolvability polyurethane, polyhydroxy butyrate, polyhydroxyvalerate, The combination or mixture of a polyalkylene OKISA rate, polyalkylene succinate, Pori (maleic acid), a chitin, chitosan and a copolymer, a terpolymer, an oxycellulose, or the above-mentioned ingredient is contained.

[0061]

Pori (glycolic acid), Pori (DL-lactic acid), Pori (L-lactic acid), and these copolymers are contained in the

example of Pori (alpha-hydroxy acid). Pori (epsilon-caprolactone), Pori (delta-valerolactone), and Pori (gamma butyrolactone) are included in the example of poly lactone.

[0062]

B. Polymer which is not biodegradability Other additives for using with the constituent of this invention are polymers which are not biodegradability. Polyacrylate, an ethylene-vinyl acetate polymer, a cellulose and a cellulosic, the cellulose acetate by which acylation was carried out and these derivatives, non-corrosive polyurethane, polystyrene, polyvinyl chloride, a polyvinyl fluoride, polyvinyl (imidazole), chloro sulfonate polyolefine, polyethylene oxide, and polyethylene are contained in the nonrestrictive example of the non-corrosive polymer which can be used as an additive.

[0063]

A polyvinyl pyrrolidone, ethylene vinyl acetate, a polyethylene glycol, cellulose acetate butylate ("CAB"), and cellulose acetate propionate ("CAP") are contained in the polymer which is not suitable biodegradability.

[0064]

C. An oil and fat The further class of the additive which can be used in the constituent of this invention is the oil and fat of nature and composition. The glyceride of a fatty acid (especially oleic acid, a palmitic acid, stearin acid, and linolic acid) is contained in the oil obtained from the seed (typically seed of nuts) of an animal or vegetation. In principle, the oil becomes still denser, so that a molecule contains many hydrogen.

[0065]

Vegetable oil, peanut oil, an inside chain triglyceride, soybean oil, almond oil, olive oil, sesame oil, peanut oil, fennel oil, camellia oil, corn oil, cotton seed oil, soybean oil (poor quality or refined material), and a medium-chain-fatty-acid triglyceride are contained in suitable nature and the nonrestrictive example of a composite oil.

[0066]

Typically, a fat is glyceryl ester of a higher fatty acid, for example, stearin acid, and a palmitic acid. These ester and those mixture are a solid-state at a room temperature, and show the crystal structure. Lard and tallow are examples. Generally, an oil and a fat increase the hydrophobicity of HVLCM and delay decomposition and incorporation of water.

[0067]

D. A carbohydrate and carbohydrate derivative Other classes of the additive which can be used with the constituent of this invention are a carbohydrate and a carbohydrate derivative. Disaccharide [, such as monosaccharide (single sugar, such as fructose and glucose (glucose) of the isomer); shoe cloth, a maltose, a cellobiose, and a lactose,]; and polysaccharide are contained in the nonrestrictive example of these compounds.

[0068]

Use of LVLCM and a HVLCM constituent A host can be medicated with a constituent given in here by various approaches that it may change with the results which should be attained. When hosts are animals, such as Homo sapiens, a medicine is part-prescribed for the patient, and is whole-body-prescribed for the patient, parenteral administration (vein administration, hypodermic administration, intramuscular administration, or intraperitoneal administration) is carried out (from membrane (opening, the rectum, a vagina, or nose)), or this constituent can be prescribed for the patient with a suitable carrier from lung tissue, for example, if it is a request. When using this constituent for administration to Homo sapiens or an animal or using it for the agricultural purpose, it can apply with injection, casting, a spray DIP, aerosol, or a coater. The aerosol or fog of this constituent can be prescribed for the patient using a suitable sprayer, using aerosol propellants (to for example, lungs, a nose, or oral cavity mucosal administration sake). (to for example, partial administration sake)

[0069]

desirable -- the medicine manufacture purpose or the veterinary medicine-purpose sake -- the constituent of this invention -- as a liquid -- injection -- or a medicine is prescribed for the patient with aerosol, a paste, or a milky lotion. If the water soluble solvent is used with the constituent when prescribing a

medicine for the patient by injection as LVLCM, the solvent will form covering of an organization which exudes in a host's aquosity liquid, and prevents the storage area of the hyperviscosity for the delivery by which the matter was controlled, or adhesion, or is made into the minimum. As explained in the top, use of the water soluble solvent in LVLCM manufacture decreases extraction time amount intentionally. In using with aerosol or a milky lotion, the little solvent in a solution evaporates on the occasion of application, and stiffens LVLCM as HVLCM. Formation of aerosol and a milky lotion can be attained using a well-known technique to this contractor. For example, Pharmaceutical Dosage Forms and Drug Delivery Systems, such as Ansel and H.C., Please refer to the 6th edition and 1995.

[0070]

Using these constituents, organization covering for protection can be formed and formation of surgical adhesion can be prevented especially. A surrounding organization or a surrounding bone can be pasted, so, hypodermically can be injected with this HVLCM like a collagen, and it can fill up structure or the deficit section with an organization. It is poured into a blemish (a burn is included) and can also prevent formation of a deep scar. The resolving time of HVLCM can be adjusted by using a polymer as an additive for example, to this HVLCM. Subsequently, biodegradation of the transplantation object formed of HVLCM is slowly carried out in a body, and it enables growth of a natural organization and a permutation with this transplantation object in the case of disappearance of this transplantation object. these constituents contain a narcotic, a painkiller, an antibiotic, and an anti-inflammatory agent suitably (however, it does not restrict to these) -- the activity matter can be included biologically.

[0071]

As mentioned above, HVLCM and the LVLCM ingredient of this invention are not used only for the emission by which matter, such as a physiological active substance to animals and plants, was controlled, and delivery, but as indicated by the United States patent application 08th / No. 044022, it is used also as a device for internal medicine or surgery (it uses into this specification by considering all the contents of this patent application as reference).

[0072]

Although the block of surgical adhesion, restoration of dead air space, induction anagenesis, hemostasis induction, organization adhesion, a scaffold, and the physic ingredient for blemishes are contained in the usefulness of the device of the constituent of this invention, it does not restrict to these. Each of these application can include emission or drug delivery of the activity matter biologically suitably. For example, the non-macromolecule ester or the mixed ester constituent as a physic ingredient for blemishes offers easily various growth factors which promote recovery of a blemish. Generally, the constituent which exists in the amount of about 99.5 to 25 percentage by weight to the total weight of a constituent for such usefulness and which has the liquid carrier ingredient of the nonaqueous solubility of a non-macromolecule can be used. These constituents can be diluted with a solvent. To this solvent Ethanol, dimethyl sulfoxide, ethyllactate, ethyl acetate, Benzyl alcohol, a triacetin, 2-pyrrolidone, N-methyl pyrrolidone, Propylene carbonate, the Glico furol, a capric acid / caprylic-acid triglyceride, One or more of benzyl benzoate, ethyl oleate, the isopropyl myristate, triethyl SHITORETO, and the aerosol propellants of arbitration are contained (in order to obtain the constituent in which implantable **** spraying is possible). It calculates based on the total weight of a constituent, and even the concentration of a liquid carrier ingredient of the nonaqueous solubility of about 10 - 90% of the weight of a non-macromolecule does not restrict to these.

[0073]

In order to block surgical adhesion, the film which blocks adhesion of a the same and different organ and which was sprayed or applied is suitable. non-macromolecule ester or a mixed ester constituent is set they to be [any of various solvents], and is blended, and the propellants (or [being accompanied by the additive] -- or it does not follow) of ethanol, ethyllactate, a N-methyl-2-pyrrolidone or the common aerosol propellants of arbitration, wood ether, or arbitration are contained in this solvent, and it can apply to it as an aerosol spray. The film generated as a result can bring about adhesion, adhesion, decomposition, porosity, or these combination.

[0074]

For dead-air-space restoration, non-macromolecule ester or a mixed ester constituent is suitable typically like the collagen for makeup restoration. In related application, non-macromolecule ester or a mixed ester constituent is useful in order to hold bone chips together at the time of fracture, and it can contain a narcotic, an antibiotic, or a growth factor suitably for the delivery which defined the aim.

[0075]

Induction anagenesis is other application of the perimeter restoration of a gear tooth for blocking migration of an epithelium etc. Advantageously, the constituent of this invention is applied from a solution. Although various growth factors and a cell reattachment factor are contained in the typical drug built into these constituents for induction anagenesis, it does not restrict to these.

[0076]

It is other usefulness in a surgery environment typically to stop hemostasis or a blood flow. The constituent of this invention is biodegradability. Although polyvinyl alcohol, a polyethylene glycol, or a carboxymethyl cellulose is contained in a suitable additive, it does not restrict to these. Ethyllactate and propylene carbonate are contained in a suitable solvent.

[0077]

Spraying of non-macromolecule ester or a mixed ester constituent or the constituent for spreading is suitable as organization adhesion for closing of a blemish (it is used with a suture or a staple as a primary sealant). Although a carboxymethyl cellulose or a polyvinyl pyrrolidone is contained in a suitable additive, it does not restrict to these. Although propylene carbonate, ethyllactate, GURIKOFURARU, dimethyl sulfoxide, 2-pyrrolidone, a N-methyl-2-pyrrolidone, and ethanol are contained in a suitable solvent, it does not restrict to these. Although an antibiotic, an anti-inflammatory compound, a painkiller, a narcotic, and a growth factor are contained in the matter [activity / target / which is incorporated for the organization adhesion with these constituents / biology], it does not restrict to these.

[0078]

Scaffold formation is other device usefulness of the constituent of this invention, and can be adapted for growth of a new organization especially. A polyvinyl pyrrolidone and TORIKARUSHIUMU phosphate are contained in a typical compound. This scaffold formation offers the matrix suitable for adhesion and growth of a bone or a nerve cell. Although a growth factor is contained in the matter [activity / target / which is built into these constituents for scaffold formation / biology], it does not restrict to these.

[0079]

other application of the constituent of this invention is the physic ingredients for blemishes (or [being accompanied by the suitable drug built into it] -- or it does not follow). This physic ingredient for blemishes functions as protecting a blemish, and promotes a recovery process. In one typical application, non-macromolecule ester or a mixed ester constituent is applied as an aerosol spray. Although an antibiotic, for example, amikacin, an anti-inflammatory compound, a painkiller, a narcotic, or a growth factor, for example, a fibroblast growth factor, is contained in the matter [activity / target / which is built into these constituents in the physic ingredient for blemishes / biology], it does not restrict to these.

[0080]

carry out for using the constituent of this invention for the emission delivery by which the activity matter was controlled biologically -- or carry out for using as a device or a transplantation object -- these constituents may have very high viscosity. As mentioned above, a HVLCM ingredient has the viscosity of 5,000cP(s) at least at 37 degrees C. In a much more special example, these HVLCM ingredients are 37 degrees C, and have about 20,000, 25,000, or viscosity higher than 50,000cP(s) higher than 15,000cP (s) still much more especially much more especially. [higher than 10,000cP]

[0081]

Example 1 The liquid of the hyperviscosity of DL-lactide / epsilon-caprolactone 75 / initial mol concentration of 25 reacted with 1,6-hexanediol.

Attached the mechanical agitator made from stainless steel which is an acetone and was rinsed in the 11. pure flask for a glass reaction, and it was made to dry under the vacuum of 0.5mmHg for 3 hours, and

dipped in the 150-degree C oil bath at coincidence. It was filled up with 197.5g (1.37 mols) DL-lactide, 52.5g (0.46 mols) epsilon-caprolactone, and 40g (0.34 mols) 1,6-hexanediol, after taking out this reactor from this bath and cooling. After addition, this reaction flask was purged 5 times with nitrogen, and was dipped in 150-degree C ****. After it seemed that most fused this mixture, it stirred slowly and the phase change was promoted. After all contents fused, the first tin solution (inside of toluene) of a 0.164M 2-ethyl hexanoic acid of 1.28mL (210micro mol) was added. Stirring was continued until this catalyst distributed over about 1 hour. This solution was maintained at 150 degrees C for 18 hours, without stirring. Subsequently the compound generated as a result was dried over 4 - 5 hours at 150 degrees C under the vacuum (<0.5mmHg), and any unreacted start ingredients were removed (low-speed stirring is applied). The product obtained as a result had the degree of peculiar ** of 0.049 dL/g (inside of CHCl₃) at 30 degrees C.

[0082]

Example 2 The liquid of the hyperviscosity of 75 / initial mol concentration of 25 of DL-lactide / glycolide reacted with 1,6-hexanediol.

The ingredient was prepared using 247.13g (1.71 mols) DL-lactide, 62.87g (0.54 mols) glycolide, and 49.6g (0.42 mols) 1,6-hexanediol using the procedure explained in full detail in the example 1. The first tin solution (inside of toluene) of a 0.141M 2-ethyl hexanoic acid of 1.84mL (260micro mol) was added following initial melting. The product generated as a result had the intrinsic viscosity of 0.058 dL/g (inside of CHCl₃) at 30 degrees C. This ingredient was a liquid at the room temperature.

[0083]

Example 3 The liquid of the hyperviscosity of 75 / initial mol concentration of 25 of DL-lactide / epsilon-caprolactone reacted with glycerol.

The ingredient was prepared using 198.14g (1.37 mols) DL-lactide, 54.8g (0.47 mols) epsilon-caprolactone, and 40g (0.43 mols) glycerol using the procedure indicated in the example 1. After initial melting, the first tin solution (inside of toluene) of a 0.154M 2-ethyl hexanoic acid of 1.36mL (210micro mol) was added. The product generated as a result had the intrinsic viscosity of 0.038 dL/g (inside of CHCl₃) at 30 degrees C. This product was a liquid at the room temperature.

[0084]

Example 4 The liquid of the hyperviscosity of 75 / initial mol concentration of 25 of DL-lactide / glycolide reacted with glycerol.

The compound was prepared using 247.33g (1.72 mols) DL-lactide, 62.87g (0.54 mols) glycolide, and 50.0g (0.54 mols) glycerol using the procedure of a publication in the example 1. The first tin solution (inside of toluene) of a 0.179M 2-ethyl hexanoic acid of 1.46mL (260micro mol) was added following initial melting. The product generated as a result had the intrinsic viscosity of 0.028 dL/g (inside of CHCl₃) at 30 degrees C. This ingredient was a liquid at the room temperature.

[0085]

Example 5 The liquid of the hyperviscosity of glycolide reacted with glycerol. Attached the mechanical agitator made from stainless steel which is an acetone and was rinsed in the 11. pure flask for a glass reaction, and it was made to dry under the vacuum of 0.5mmHg for 3 hours, and dipped in the 150-degree C oil bath at coincidence. It was filled up with 174g (1.5 mols) glycolide and 92g (1.0 mols) glycerol, after taking out this reactor from this bath and cooling. After addition, this reaction flask was purged 5 times with nitrogen, and was dipped in 150-degree C ****. After it seemed that that most fused this mixture, it stirred slowly and the phase change was promoted. After all contents fused, the first tin solution (inside of toluene) of a 0.164M 2-ethyl hexanoic acid of 1.28mL (210micro mol) was added. Stirring was continued until this catalyst distributed over about 1 hour. This solution was maintained at 150 degrees C for 18 hours, without stirring. Subsequently the compound generated as a result was dried, stirring over 4 - 5 hours at a low speed at 150 degrees C under a vacuum (<0.5mmHg), and any unreacted start ingredients were removed.

[0086]

Example 6 The hyperviscous liquid of epsilon-caprolactone reacted with 1-dodecane.

The ingredient was prepared using 513g (4.5 mols) epsilon-caprolactone and 93g (0.5 mols) 1-dodecane

using the procedure indicated in the example 5. After addition of a reagent, the first tin solution (inside of toluene) of a 0.154M 2-ethyl hexanoic acid of 1.36mL (210micro mol) was added. It was made to go on, as this reaction was indicated in the example 5, and refined like a publication there.

[0087]

The approach of using the constituent of this invention is illustrated below.

[0088]

Example [] A CAPROL 10G40 (deca glycerol tetra-oleate) were dissolved in benzyl benzoate by the weight ratio of 50:50. The bupivacaine was dissolved in this mixture by 8.75wt% concentration. The drop with a weight of about 100mg was dropped into the test tube containing the buffer solution of 40mL(s). The sample of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. These samples were analyzed by 265nm by UV-visible spectrophotometry, and the concentration of the bupivacaine in each buffer-solution sample was measured. At the time of 4 hours, less than [of the bupivacaine in a drop / 7.5wt%] was emitted into the buffer solution. About 24.0 wt (s)% of the bupivacaine was emitted at the time of 48 hours. The cumulative emission profile was shown in drawing 1.

[0089]

Example [] B the 1,6-hexanediol lactate epsilon-hydroxy caproic acid generated in the example 1 was dissolved in N-methyl pyrrolidone by the weight ratio 70:30. Subsequently, the 10wt% bupivacaine was added and dissolved in this mixture. The drop with a weight of about 100mg was made dropped at the buffer solution of 40mL. The sample of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. The buffer-solution sample was analyzed by 265nm by UV-visible spectrophotometry, and the concentration of the bupivacaine in each buffer-solution sample was measured. About 4.1 wt(s)% of the bupivacaine contained in the dropped drop at the time of 4 hours was emitted. About 8.6 wt(s)% of the bupivacaine was emitted at the time of 24 hours. The cumulative emission profile was shown in drawing 1.

[0090]

Example [] C the glycerol lactate glycolate prepared according to the example 4 was dissolved by the weight ratio of 70:30 into ethanol. Subsequently, 10wt% estradiol was added to this mixture as suspension. It examined, after homogenizing this compound, and suitable mixing was ensured. The drop of this compound was poured in into the test tube containing the buffer solution. Glycerol lactate glycolate was dropped and estradiol formed the storage area emitted slowly. The sample of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. The buffer-solution sample taken out from each of these test tubes was analyzed by 280nm by UV-visible spectrophotometry, and the estradiol concentration in each sample was measured. The percent of the estradiol emitted from the drop was calculated using the concentration which carried out assay. Drawing 2 shows the cumulative emission profile of estradiol.

[0091]

Example [] D the 1,6-hexanediol lactate glycolate prepared according to the example 2 was dissolved by the weight ratio of 80:20 into propylene carbonate. 10wt(s)% progesterone was made to incorporate as suspension in this mixture. It examined, after homogenizing this compound, and suitable mixing was ensured. The compound generated as a result was analyzed and the Inn vitro dissolution profile was measured. The drop of this compound was poured in into the test tube containing the buffer solution. 1,6-hexanediol lactate glycolate was dropped and progesterone formed the storage area emitted slowly. The sample of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. These buffer-solution samples were analyzed by 244nm by UV-visible spectrophotometry, and the drug concentration in each sample was measured. The percentage of the progesterone emitted from the drop was calculated using the concentration which carried out assay. This cumulative emission profile was shown in drawing 3.

[0092]

Example [] E the glycerol lactate epsilon-hydroxy caproic acid prepared according to the example 3 was dissolved in the polyethylene glycol (PEG) 400 by the weight ratio of 36:64. The lysozyme was ground

using the mortar and the pestle and the generated powder was incorporated by 10wt(s)% concentration as suspension into this mixture. This compound was thoroughly mixed using the spatula. The sample of the volume of about 500microL of this compound was poured into three test tubes containing the buffer solution of ten mL(s) each. The aliquot (8mL) of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. Each sample of the buffer solution containing a lysozyme was analyzed using the reagent kit for micro BCA protein assays, and the protein content in this dissolution sample was measured. The percent of the lysozyme emitted from the drop was calculated using this lysozyme concentration that carried out assay. The cumulative emission profile was shown in drawing 4.

[0093]

Example [] F CAPROL 6G2O (hexa glycerol dioleate) was dissolved in benzyl benzoate by the weight ratio of 25:75. The lysozyme was ground using the mortar and the pestle and the generated powder was incorporated by 10wt(s)% concentration as suspension into this mixture. This compound was thoroughly mixed using the spatula. The sample of the volume of about 500microL of this compound was poured into three test tubes containing the buffer solution of ten mL(s) each. The aliquot (8mL) of the buffer solution was taken out at the specific time, and it replaced with the fresh buffer solution. Each sample of the buffer solution containing a lysozyme was analyzed using the reagent kit for micro BCA protein assays, and the protein content in this dissolution sample was measured. The percent of the lysozyme emitted from the drop was calculated using this lysozyme concentration that carried out assay. The cumulative emission profile was shown in drawing 4.

[0094]

Example [] G two sorts of solutions made to dissolve a 1,6-hexanediol lactate epsilon-hydroxy caproic acid (for it to prepare according to an example 1) and 1,6-hexanediol lactate glycolate (for it to prepare according to an example 2) in a polyethylene glycol (PEG) 400 by the weight ratio of 34:66 and 33:67, respectively were prepared. The drop of each compound was poured into the test tube containing deionized water, and a 1,6-hexanediol lactate epsilon-hydroxy caproic acid and 1,6-hexanediol lactate glycolate were dropped at the bottom of these test tubes. These drops held those configurations over the long period of time from one week.

[0095]

Example [] H the compound listed to the following table was prepared using the ester prepared in the examples 1-4. In each case, mixture produced the uniform solution.

[Table 1]

エステル	溶剤	エステル：溶剤(重量比)
1,6-ヘキサンジオールラクテート グリコレート	エタノール	80 : 20
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	エタノール	80 : 20
グリセロールラクテートエ- ヒドロキシカブロ酸	エタノール	80 : 20
グリセロールラクテートグリコレート	エタノール	80 : 20
1,6-ヘキサンジオールラクテート グリコレート	プロピレンカーボネート	80 : 20
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	プロピレンカーボネート	80 : 20
グリセロールラクテートエ- ヒドロキシカブロ酸	プロピレンカーボネート	80 : 20
グリセロールラクテートグリコレート	プロピレンカーボネート	80 : 20
1,6-ヘキサンジオールラクテート グリコレート	ポリエチレングリコール (PEG)400	36 : 64
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	ポリエチレングリコール (PEG)400	34 : 66
グリセロールラクテートエ- ヒドロキシカブロ酸	ポリエチレングリコール (PEG)400	33 : 67
グリセロールラクテートグリコレート	ポリエチレングリコール (PEG)400	37 : 63
1,6-ヘキサンジオールラクテート グリコレート	N-メチル-2- ピロリドン	80 : 20
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	N-メチル-2- ピロリドン	80 : 20

[Table 2]

エステル	溶剤	エステル:溶剤(重量比)
グリセロラクテートエ- ヒドロキシカブロ酸	N-メチル-2- ピロリドン	80:20
グリセロラクテートグリコレート	N-メチル-2- ピロリドン	80:20
1,6-ヘキサンジオールラクテート グリコレート	ベンジルベンゾエート	70:30
1,6-ヘキサンジオールラクテート グリコレート	グリコフロール	70:30
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	ジメチルスルホキシド	70:30
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	プロピレングリコール	50:50
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	ベンジルベンゾエート	70:30
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	グリコフロール	70:30
1,6-ヘキサンジオールラクテートエ- ヒドロキシカブロ酸	ジメチルスルホキシド	70:30
グリセロラクテートエ- ヒドロキシカブロ酸	プロピレングリコール	50:50
グリセロラクテートエ- ヒドロキシカブロ酸	ベンジルベンゾエート	70:30
グリセロラクテートエ- ヒドロキシカブロ酸	グリコフロール	70:30
グリセロラクテートエ- ヒドロキシカブロ酸	ジメチルスルホキシド	70:30
グリセロラクテートグリコレート	プロピレングリコール	50:50

グリセロ-ラクテートグリコレート	グリコフロール	70 : 30
グリセロ-ラクテートグリコレート	ジメチルスルホキシド	70 : 30
グリセロ-ラクテートグリコレート、酸 末端	エタノール	70 : 30
グリセロ-ラクテートグリコレート、酸 末端	プロピレンカーボネート	70 : 30
グリセロ-ラクテートグリコレート、酸 末端	N-メチル-2-ピロリドン	70 : 30
グリセロ-ラクテートグリコレート、酸 末端	プロピレングリコール	50 : 50
グリセロ-ラクテートグリコレート、酸 末端	グリコフロール	70 : 30
グリセロ-ラクテートグリコレート、酸 末端	ジメチルスルホキシド	70 : 30

[0096]

Example I The 10wt% solution (inside of the constituent containing SAIB/NMP of 70:30) of the 5.33g bupivacaine prepared as indicated by U.S. Pat. No. 5,747,058 was added to the container for aerosol. 14.32g propellants R-143a (1, 1, 1, 2-tetrafluoro ethane) was added. This mixture formed the solution sprayed easily, without foaming.

[0097]

Example [] J the 10wt% solution (inside of the constituent containing SAIB/NMP of 70:30) of the 5.44g bupivacaine prepared as indicated by U.S. Pat. No. 5,747,058 was added to the container for aerosol. 16.55g propellants [14.32g] R-143a (1, 1, 1, 2-tetrafluoro ethane) was added. This mixture formed the solution sprayed easily, without foaming.

[0098]

Example [] K the bupivacaine base of 0.87 g was added to the aerosol container. 2. 8.47g SAIB / propylene carbonate solution (70:30) containing a 5wt% biodegradability polymer (65:35 DLPLG) were added to this container. 0.98g ethanol was added in order to help the dissolution of a drug. Once it dissolved, about 16g propellants R-134a (1, 1, 1, 2-tetrafluoro ethane) was added. This mixture formed the solution sprayed easily, without foaming.

[0099]

Example [] L SAIB was dissolved in propellants 134a (1, 1, 1, 2-tetrafluoro ethane) and 227 (1, 1, 1, 2, 3, 3, and 3-heptafluoro propane) on level (5 and 10wt(s)%). The transparent solution was formed.

[0100]

Example [] M the further example was performed, and in order to offer continuous emission of a lysozyme, the controlled new emission system using hyperviscous compound shoe cloth acetate

ISOBUCHIRETO (SAIB) was evaluated. A little solvent changes SAIB into the liquid with which it can inject easily. Once it is injected, a solvent will diffuse and a hyperviscous biodegradable transplantation object will be formed. An emission profile is changeable by using a different solvent and a different additive.

[0101]

SAIB/solvent mixture containing solvent ethyllactate, a N-methyl-2-pyrrolidone (NMP), MIGLYOL 810, and benzyl benzoate were made to suspend the ground lysozyme (10wt%). Three Pori (DL-lactide-KOGURI corridor) polymers which have an acid, ester, or a PEG end group were evaluated as an additive. In order to measure an emission rate, after pouring the drop of a compound into the test tube into which the buffer solution of pH6.24 was put, it incubated at 37 degrees C in the shaker. At a certain time, the aliquot of the buffer solution was taken out and it replaced with the fresh buffer solution. The lysozyme concentration in the buffer solution was measured by BCA protein assay. Protein activity was measured using the enzyme assay which measures the lysis of the suspension of micrococcus RIZODAIKUCHIKASU (lysodeikticus) by spectrophotometry. Reduction with an absorbance of 450nm was recorded as a function of time amount (this is directly related to activity lysozyme concentration).

[0102]

At the time of 6 hours, emission attained to 4.5wt(s)% of 40:60 SAIB / ethyllactate compound (107.6**6.1% activity) from 1.3wt(s)% of the 70:30 SAIB/NMP compound (110.3**5.0% activity). The percent emitted in the 7th day attained to 46.7% (88.9**6.8% activity) to 96.4% of 70:30 SAIB/MIGLYOL (107.6**7.0% activity) of 40:60 SAIB / ethyllactate. 0.5wt(s)% to each SAIB/NMP compound of these three polymers of addition did not have significant effect on the emission profile.

[0103]

These results show that the above-mentioned SAIB / solvent delivery system can give continuous emission of the protein of an active state, and that the emission profile of the range where the emission rate is adjusted can be given.

[0104]

Example [] N the further example was performed and the effectiveness of the variable of a compound over rip-off TAKUSERU of the chemotherapeutic drug from a compound and the emission of 5-fluorouracil (5-FU) based on a SAIB delivery system was evaluated. From the above-mentioned publication, it will be understood that a SAIB delivery system uses as an excipient the shoe cloth derivative of shoe cloth acetate ISOBUCHIRETO (SAIB) and the water-insoluble nature esterified completely. By MIGLYOL, a small amount of solvent, for example, ethanol, ethyllactate, propylene carbonate, or DMSO addition, it can be blended as a liquid of the viscosity of low - a medium, and generates the compound with which it can inject easily.

[0105]

The solution of SAIB in a suitable solvent can be prepared without following with incorporation of an additive. The active ingredient was measured, it put into the test tube, SAIB/mixture was added, it mixed thoroughly, and a solution or suspension was generated by desired drug combination. It was dropped into the buffer solution by pouring in the single drop of this mixture using a standard syringe and a standard hypodermic needle. The sample was maintained at 37 degrees C in the shaker, and it sampled periodically, and analyzed per activity emission by UV-visible spectrophotometry. Rip-off TAKUSERU and a 5-FU sample were analyzed by 232nm and 266nm, respectively.

[0106]

The effectiveness of drug combination was evaluated about rip-off TAKUSERU. Drug combination of 5, 25, and 50 mg/mL was compared. Seven days after, the cumulative emission about these three drug combination was 106.4%, 85.9%, and 33.8%, respectively. The effectiveness of a surfactant additive was also evaluated. The rip-off TAKUSERU compound of 25 mg/mL and the 5-FU compound (both inside of SAIB/EtOH of 85:15) of 10 mg/mL were created, and 5wt(s)% Cremophor(trademark) EL was added. Addition of this surfactant increased the emission rate to both compounds. The percent emitted from this rip-off TAKUSERU compound is the Inn vitro, and increased 56.0 to 77.0% two days after. Similarly, the percent emitted from the 5-FU compound increased 80.6 to 106.0% two days after. The

second surfactant Pluronic(trademark) L-101 was added to 10 mg/mL 5-FU (inside of the SAIB/EtOH compound of 85:15). This surfactant also increased the burst size 80.6 to 102.0% two days after.

[0107]

The emission rate from the SAIB delivery system of drugs, such as rip-off TAKUSERU and 5-fluorouracil, can be adjusted with the variable of a compound including the class of drug combination and surfactant. It can change in several days from the persistence time mist beam of the emission from this system of these drugs, and several hours, and becomes the still shorter persistence time by addition of still lower drug combination and a surfactant.

[0108]

Example [] Other examples were performed and the potentia of a SAIB delivery system which gives the emission extended after internal use of the anti-retrovirus agent used for the therapy of HIV infection was evaluated. As mentioned above, the shoe cloth derivative of shoe cloth acetate ISOBUCHIRETO (SAIB) and the water-insoluble nature esterified completely is used for a SAIB delivery system as an excipient.

[0109]

Zidovudine (AZT) and dideoxy SHITOJIN (ddC) suspension were prepared by mixing a drug with SAIB / solvent solution (the thing accompanied by a cellulose excipient, and thing by which it is not accompanied). The heat seal of each about 1g compound was filled up with and carried out to the elasticity gelatine capsule. The dissolution profile was measured at the paddle speed of 50rpm using Apparatus2 and MethodB (USP XXIII). Each gel cap was placed into the separate dissolution container, and the sample of the buffer solution in each container was obtained at the time of 0.25, 0.5, 1, 2, 3 and 6, and 24 hours. These samples were analyzed by 266 and 272nm about AZT and a ddC drug content with the Perkin Elmer Lambda 20 UV-visible spectrophotometer, respectively.

[0110]

It can adjust easily by using a solvent which is different in a SAIB delivery system in emission of AZT and ddC. By using the combination of 70:30SAIB(s) / MIGIRORU (trademark) 810, the emitted cumulative percent in the time of 2 hours was 104.1% about the 11.1wt%AZT compound, and was 74.2% about 0.225wt%ddC. When it compared and the combination of SAIB/EtOH of 85:15 was used, 71.2% of the drug in this AZT compound was emitted, and 59.5% of the drug in a ddC compound was emitted. Emission can be adjusted also by changing drug combination. combination [activity / compound / of 85:15 / SAIB/EtOH] -- up to 11.1 to 22.2wt(s)% -- twice -- were-izing and the emitted cumulative percent increased from 71.2% to 93.8%. The use for adjusting emission of polymer additives and cellulose acetate butylate (CAB) was also evaluated. About 11.1wt%AZT in a 85:15 SAIB/EtOH compound, addition of 0.02 and 0.2wt% CAB decreased the burst size in 2 hours from 71.2% to 25.6% and 7.6%, respectively. About 0.225wt% ddC in a 85:15 SAIB/EtOH compound, addition of 0.5 and 1.0wt% CAB decreased the burst size in 2 hours from 59.5% to 39.4% and 13.5%, respectively.

[0111]

It is shown that it is adjusted and the compound of this SAIB delivery system deals in these data so that the dissolution profile of the range which is for AZT and ddC may be given. By giving the emission by which these active substances were controlled, this system can reduce the number of the pills for which per day is needed, and can reduce a manufacturing cost, and can improve a patient's compliance.

[0112]

In this way, although indicated this invention, its deformation, and an alteration object will probably be clear to this contractor, they will be understood to be a thing in an attached claim.

[Brief Description of the Drawings]

[Drawing 1]

It is the graph which shows the cumulative emission profile from a 1,6-hexanediol lactate epsilon-hydroxy caproic acid from the deca glycerol tetra-oleate by this invention of the bupivacaine.

[Drawing 2]

It is the graph which shows the cumulative emission profile from the glycerol lactate glycolate by this invention of estradiol.

[Drawing 3]

It is the graph which shows the cumulative emission profile from the 1,6-hexanediol lactate glycolate by this invention of progesterone.

[Drawing 4]

It is the graph which shows the cumulative emission profile from the hexa glycerol dioleate by this invention and glycerol lactate glycolate of a lysozyme.

[Translation done.]

* NOTICES *

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1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DRAWINGS

[Drawing 1]

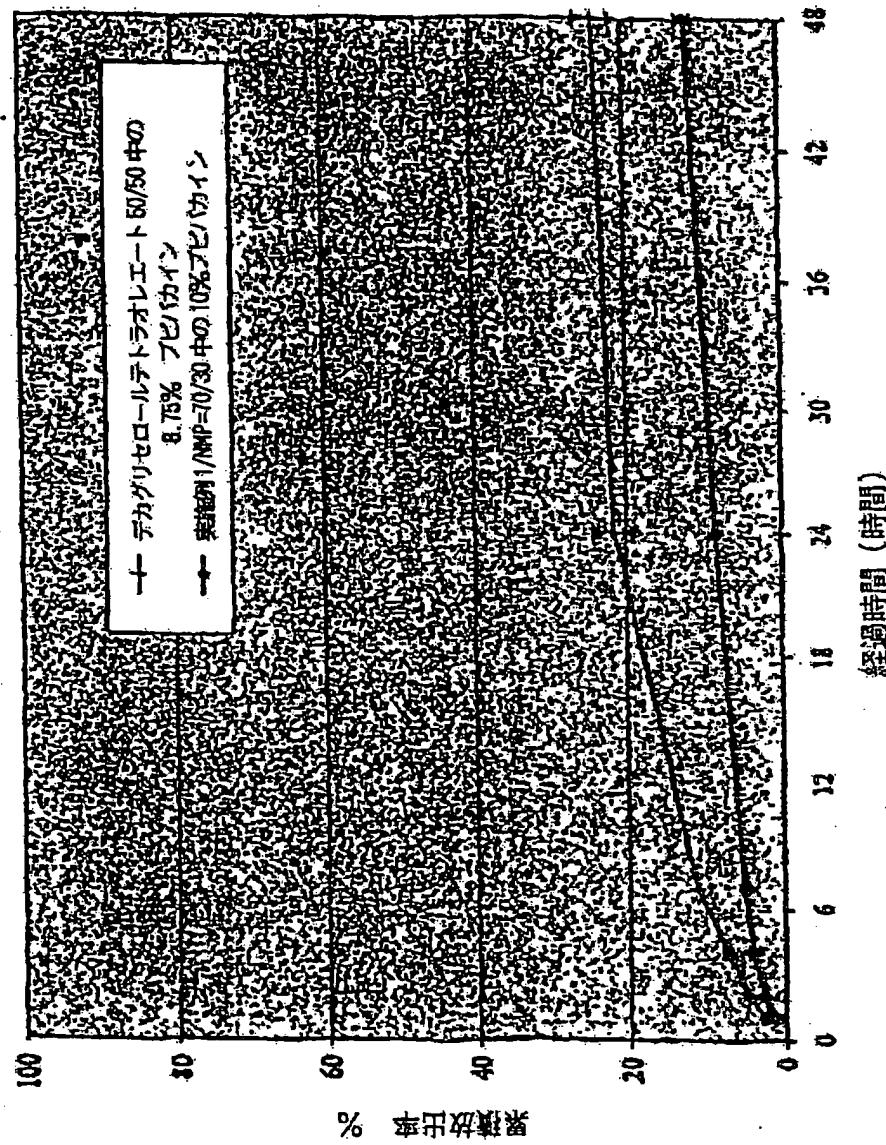
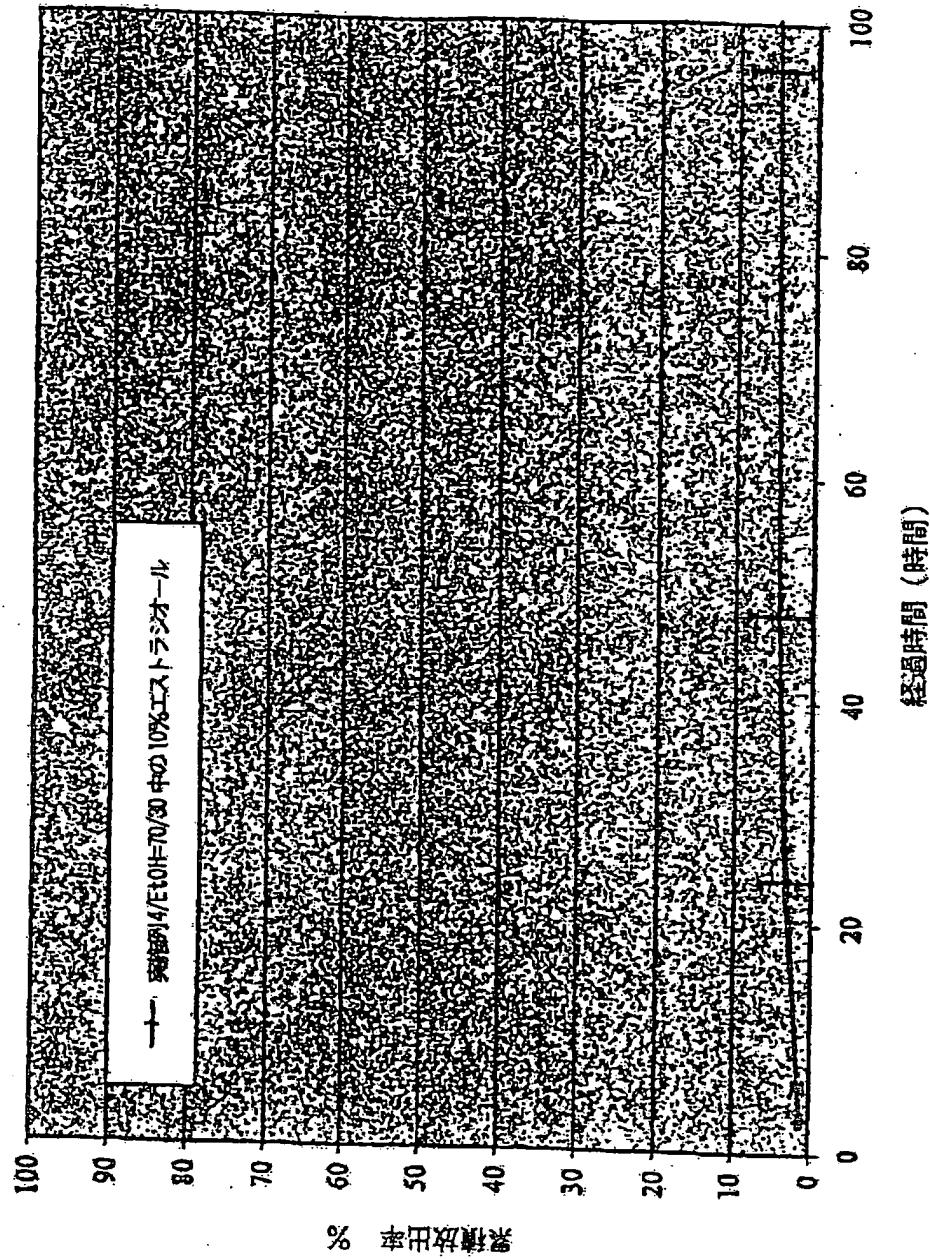


Fig. 1

[Drawing 2]

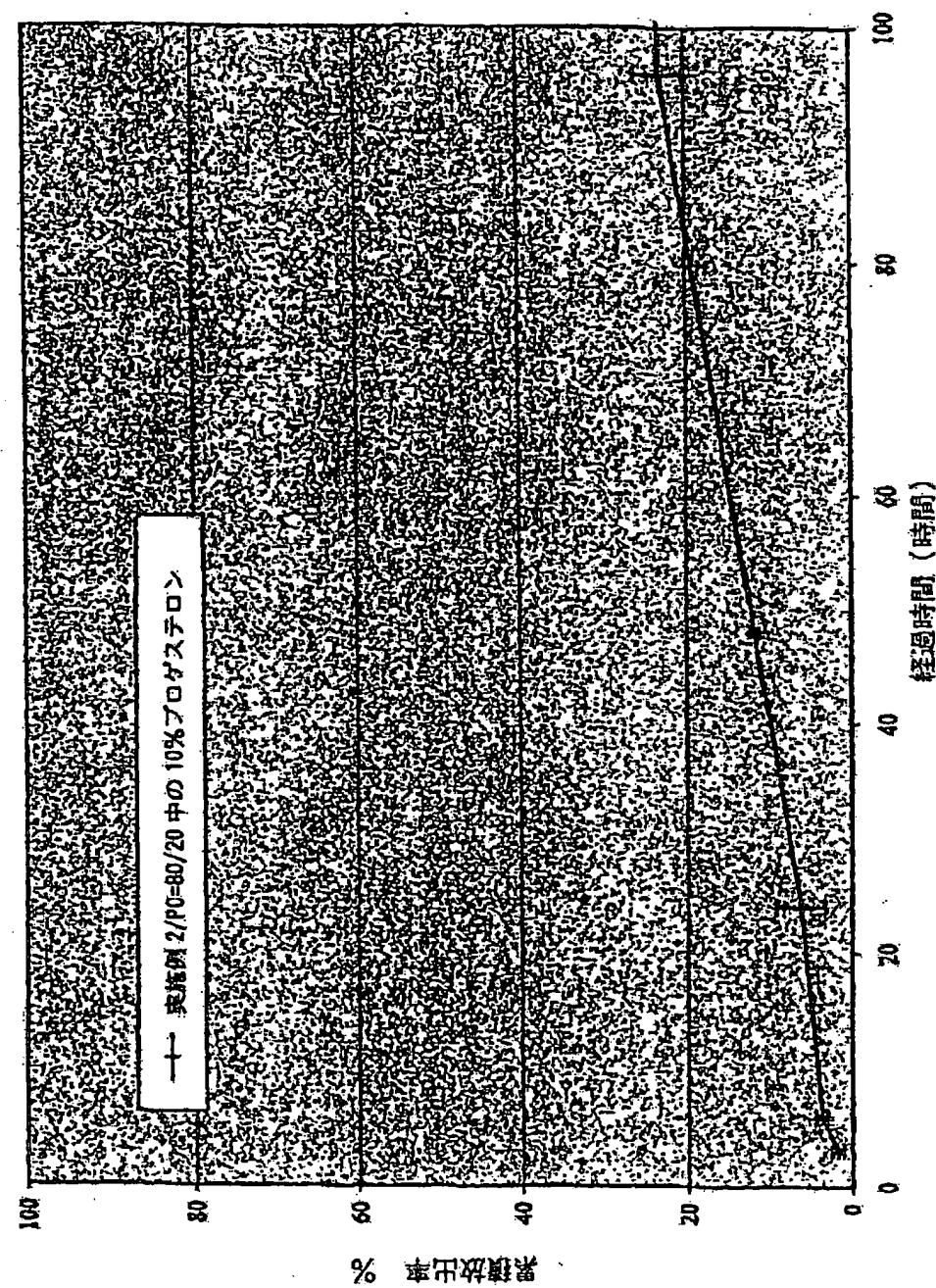
Fig. 2
生体外におけるエストラジオールの
生分解性エステル/溶媒配合物からの放出



[Drawing 3]

Fig. 3

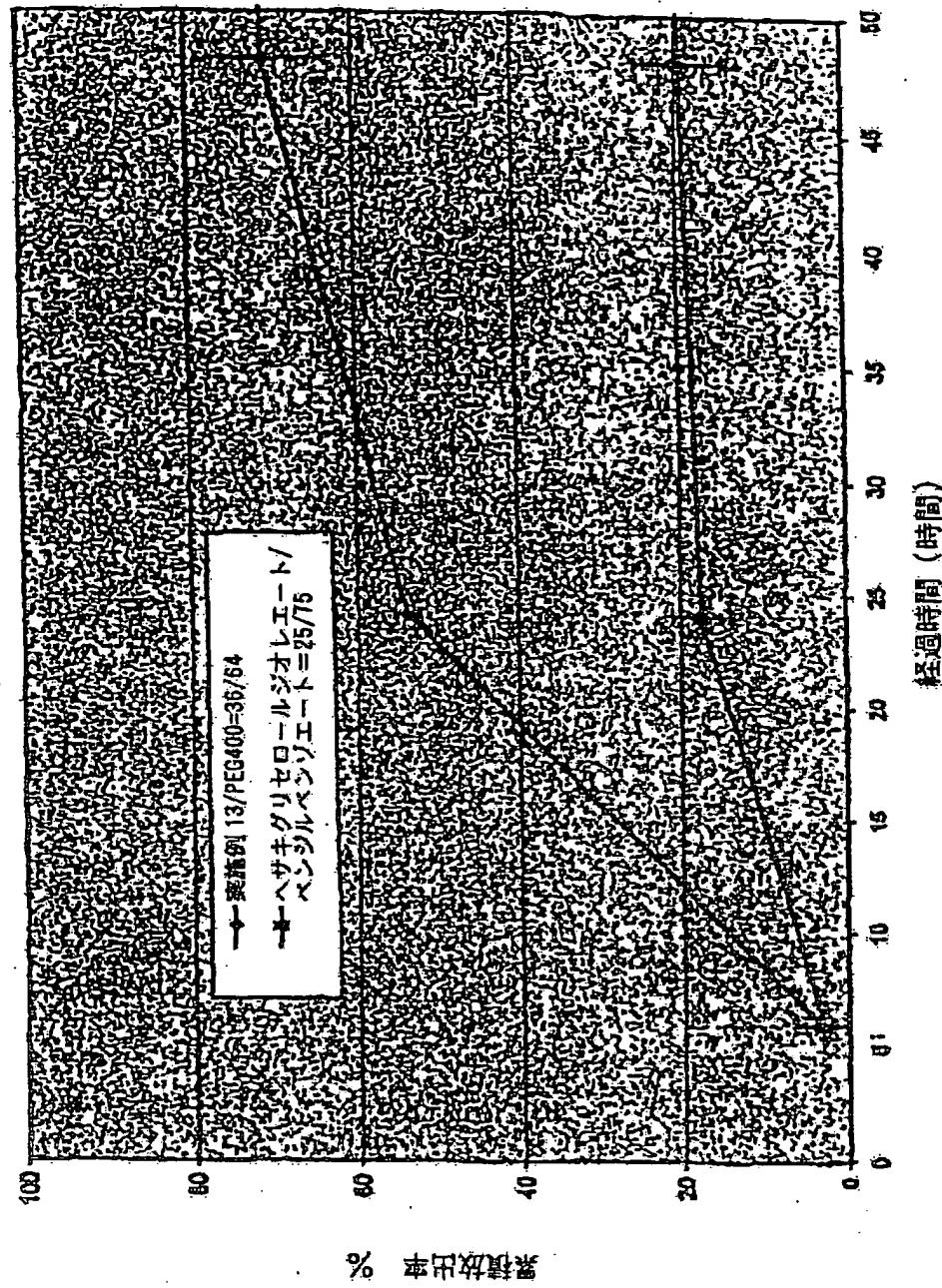
生体外におけるプロゲステロンの生分解性エステル/溶媒配合物からの放出



[Drawing 4]

Fig. 4

生体外における懸濁放出配合物からの10%リソチームの放出



[Translation done.]